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THE MEDICAL JOURNAL OF AUSTRALIA

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ANOVULATORY MENSTRUATION.[1]

By R. MACKEY,

Major, Australian Army Medical Corps, Australian Imperial Force.

THE investigation of women for the causal factors of sterility invariably discloses a certain percentage who do not ovulate, even though periodic uterine hæmorrhage may occur. The actual percentage who exhibit this phenomenon is not yet definitely agreed upon; Rock[1] and his associates hold that 9·1% of women complaining of sterility show evidence of occasional anovulatory menstruation; Mazer, Israel and Kocher[2] state that "thirty percent of sterile women who possess no abnormality have cyclic uterine bleeding clinically indistinguishable from normal menstruation, from an endometrium totally lacking in the usual secretory changes". Other authorities quote figures varying from 10% to 48%, most of which are based on the examination of women whose primary and generally single presenting symptom is sterility. The presence of such cycles without ovulation was proved to exist in the *Macacus rhesus* monkey by Hartman and Corner, who also noted that both anovulatory and ovulatory cycles were followed by the same amount of hæmorrhage. Moreover, such cycles appear to be quite a normal occurrence in these monkeys. Gradually the application of this principle to the human female has been investigated, and it is now accepted almost without dispute. Novak[3] states that "endometrial biopsy when employed at the very beginning of a menstrual flow has in many instances revealed an endometrium which shows not the slightest evidence of the secretory changes commonly accepted as the criterion of corpus luteum activity, and therefore of ovulation".

[1] This paper is based on work done and observations made as pathologist to the sterility clinic of the Women's Hospital, Sydney.

Determination of Ovulation.

The presence or absence of ovulation is determined from the microscopic appearance of the endometrium in the premenstrual phase. The tissue is removed with the biopsy curette in the clinic at any time from the seventh day preceding the onset of menstruation to four hours after the establishment of the flow (for the technique, *vide infra*). Small pieces of tissue are removed, preferably from the anterior and posterior walls at the fundus, and they are immediately fixed in formalin acetic acid and alcohol fixative, or if evidence of glycogen secretion is desired, in Carnoy's fluid. Sections are stained with indigo-carmine (Best's stain) and hæmatoxylin and eosin. The size of the piece of tissue removed should not be a deterrent; on occasions a section a few millimetres in diameter has been sufficient to provide a diagnostic picture.

Ovulation is now assumed to occur in normal ovulating adults on or about the thirteenth to the fifteenth day from the commencement of the cycle, and the changes seen in the normal endometrium from the assumed date of ovulation are quite striking.[4] On the fifteenth day vacuolization of the cytoplasm occurs in the epithelial cells, most prominently in those lining the superficial glands, and the nuclei appear to migrate towards the surface of the cells, leaving a clear zone at the base. This effect is maximal on the seventeenth day, when the nuclei are normally lying in a row, each one towards the centre of its own cell. The next nuclear move is towards the base, where they return about the nineteenth day. Secretion begins about the seventeenth day, and by the twenty-first is well advanced. As the nuclei migrate towards the base, clearing of the superficial cytoplasm occurs, the cell swells, and finally the superficial margins break down and active secretion occurs into the lumina of the glands. These glands dilate, the swollen cells give them a serrated or saw-toothed appearance in cross section, and they become tortuous. The stromal changes are just as distinct. On or about the eighteenth day small patches of œdema appear in the more superficial areas, and the stromal nuclei, which

hitherto had been closely packed and surrounded by very little cytoplasm, gradually become separated, until by the twenty-first day each is discrete from its fellow. The next change is an increase in the cytoplasm; this first occurs in the cells surrounding the small arterioles on the twenty-third day, and by the twenty-sixth day the œdema is replaced by a sheet of stromal cells with large, pale nuclei and abundant cytoplasm. Just before menstruation commences the superficial layer becomes almost solid, and there is a striking resemblance of these stromal cells to decidual cells. The glands at this time are sometimes dilated, contain varying amounts of secretion, and are lined by cuboidal epithelium.

The foregoing changes may be taken as presumptive evidence of ovulation for that particular cycle, if they are seen in an endometrium from which material for biopsy has been taken in the week preceding the occurrence of menstruation, and if the microscopic changes agree with the day of the cycle. This commonly is the case; but in some cases the endometrium exhibits secretory changes which do not correspond with the cyclic date. These changes are not regarded as anovulatory, but due rather to (i) late ovulation or (ii) a poor luteal response, as in the majority of these cases the evidence of secretion has been minimal.

The endometrium in anovulatory cycles shows changes which are just as characteristic as the normal secretory changes. The glands are non-tortuous and lined by tall columnar cells, sometimes two or three deep, showing stratification or pseudo-stratification. The nuclei of the epithelial cells are large, deeply staining and oval; mitotic figures and nucleoli are often plainly seen. There is absolutely no evidence of secretion. In the stroma the cells are closely packed, and the nuclei are small and darkly staining and surrounded by very little cytoplasm. Œdematous patches and small hæmorrhages are the exception more than the rule. An occasional gland may appear enlarged and dilated with a flattened epithelium and changes simulating simple hyperplasia, the well-developed form of which is occasionally seen in these biopsies.

More recent investigators[7][8] have devised electrical methods for determining the time of ovulation, whilst Venning and Brown[9] found increasing quantities of pregnandiol excreted in the urine during the latter half of the menstrual cycle. As pregnandiol appears to be the urinary excreted form of luteal hormone, the hypothesis that the rise in excretion corresponds to the formation and activity of the *corpus luteum* appears to be sound. This discovery has been confirmed by other workers,[10] and deficiencies in excretion have been correlated with absence of or deficiency in the endometrial secretory changes. The method used for the estimation of pregnandiol is a gravimetric one and requires a trained biochemist. It offers, however, a further check on ovarian function and ovulation, and should be made if possible.

Clinical Picture of Anovulatory Menstruation.

The occurrence of anovulatory cycles at either end of the menstrual history of a woman seems to be established; the irregularity of the cycles at the menarche and menopause may be an indication of early and late anovular phases. The fact that an ovum has not been produced may be totally unsuspected in some cases, as the periodicity and amount of flow may show no deviation from normal. In a series of 36 cases recorded by Rock,[1] four fell into such a category, and the cycles were proven to be anovular only by biopsy. Irregularities in menstrual history are more often observed, and as a general rule it is taken that any patient who complains of sterility and has had irregularities in menstrual history must be suspected of anovulation. Oligomenorrhœa, amenorrhœa, irregular periods, metrorrhagia and polymenorrhœa are the usual findings which occur with the greatest frequency in patients with persistent anovulation. Some regularly ovulating women occasionally fail to ovulate in odd cycles which cannot be differentiated except by biopsy, and in the same fashion an occasional ovulatory cycle is sometimes interposed in a well-established anovulatory cycle, no clinical differentiation being possible. Occasionally patients show characteristics indicative of pituitary or adrenal dysfunction. These may be manifested by such signs as hirsutism of a male type, abnormal increase in fat deposits of the girdle, mons and mammary type, deep voice and frigidity.

The diagnosis of anovulation cannot be made on the result of one biopsy, nor can success be claimed for any form of treatment which promotes a secretory action or even results in pregnancy in one case only.

Treatment.

In established cases treatment is now regarded as unsatisfactory. In the *Macacus rhesus* monkey it appears quite an easy matter to induce ovulation by hormonic means, and in the lower vertebrates it seems to become progressively easier; but in *Homo sapiens* the problem is very difficult. The primary failure appears to be in the functional control of the anterior pituitary in ripening the follicle and causing it to rupture. The exhibition of hormones in treatment has been tried with the aim of assisting this function. Prolan-containing pregnancy urine principles were suggested by Novak and Hurd[10] in 1931; but the fact that the ovary did not respond by follicle formation and extrusion of an ovum has since been confirmed by many workers.[11][12] Novak later stated that "the evidence seems conclusive that the pregnancy urine principles never produce follicle stimulation in the human ovary and that they are not capable of bringing about the extensive luteinisation seen in the ovaries of some animals". The use of anterior pituitary-like hormones recovered from the serum of pregnant mares has called forth favourable reports in isolated cases,[13][14] in which secretory phases of the endometrium and also pregnancy have occurred. The question in these cases is whether the results may not have been spontaneous, as so often happens. Treatment was by the administration of large doses of the hormone by intramuscular and intravenous routes at times which would normally correspond to the proliferative phase of the cycle. The repeated daily doses are not without danger. In the Women's Hospital clinic no positive results were obtained with this treatment. In a report by the Council of Pharmacy and Chemistry of the American Medical Association[15] the following statement is made:

> Further experimentation is required under suitable conditions and by investigators whose special training qualifies them for appropriate study of this material. Until the status of gonadotropin from serum of pregnant mares may be properly evaluated, physicians are cautioned that use of this substance is still in the early experimental stage, that claims made by the manufacturers are without satisfactory foundation and that additional publication of more satisfactory evidence is necessary before this substance should be used in general practice.

The editor of the "Year Book of Obstetrics and Gynecology" (1941) remarks that "thus far chorionic gonadotropins, certainly those from pregnant mare serum, have been of little or no practical assistance in the treatment of ovarian dysfunctions". Geist, Gains and Salmon,[16] investigating the effect of gonadotropins upon the human ovary, used hypophyseal, chorionic and pregnant mares' serum, and combinations of chorionic and hypophyseal serum, chorionic and equine serum and chorionic serum and stilbœstrol. They concluded on an analysis of 91 cases that while the available gonadotropins may stimulate granulosa and *theca interna* cells, in follicles undergoing atresia which are still capable of response, they apparently do not induce follicle stimulation or stimulate the development to maturity and ovulation of follicles containing normal ova.

The effectiveness of small doses of Röntgen therapy in the stimulation of refractive ovaries has not yet been estimated fully. Silbernagel and Fidler,[17] chiefly by the use of glandular products and Röntgen therapy, report 54·4% successes in a series of sterility cases. The actual number of cases of anovulation in this series is not known.

Recent reports quoted in "Recent Advances in Obstetrics and Gynæcology" (fifth edition, page 330) give promising results from irradiation to the pituitary and ovaries in

cases of sterility associated with deficient menstruation, hypermenstruation and regular menses. In some of these cases menstruation must have been anovular.

It can be seen, then, that the hormonic treatment of anovulation is still without avail. The hormones which are at present obtainable appear to have little or no effect on the condition, and it will be only by further trial and experimentation on the human being with suitable controls that success may in future be obtained in suitable cases.

Technique of Endometrial Biopsy.

Endometrial biopsy is carried out in the week which is estimated to be the one prior to the onset of menstruation. It is not attempted in the presence of any degree of vaginal infection. After a complete vaginal examination the vagina is swabbed out with "Dettol" solution and dried; the cervix is pulled down with a volsellum and painted with *Tinctura Iodi Mitis*. A sound is then passed into the uterus to determine its length and situation. The endometrial biopsy curette is then gently and slowly inserted into the cavity of the uterus. It may take three to five minutes to overcome resistance at the internal os. Scrapings are taken from the fundus and the anterior and posterior walls and deposited directly into the fixative. If the cervical canal is very narrow or stenosed, the insertion of a small swab of cotton wool impregnated with a 20% solution of cocaine, which is left for five minutes, will allow the operation to proceed painlessly. At the Women's Hospital clinic it was found that approximately 20% of patients could not be treated thus as out-patients, owing to cervical stenosis; consequently they were admitted to hospital and the biopsy was performed under anæsthesia after a Rubin test. A few patients complained of lower abdominal pain or of a feeling of faintness; but in over 200 biopsies no serious complications occurred.

Acknowledgements.

Acknowledgements are made to Dr. Alan Grant, of the Women's Hospital, Sydney, for suggesting that an article be written on this little-appreciated subject, and for most helpful advice from the clinical side. His alternative suggestion for a paper, "Endometrial Biopsy: A New and Neglected Method of Diagnosis", was to include a discussion on functional uterine bleeding; but the exigencies of war have prevented the completion of the article in this light and also the presentation of the statistics of anovulatory menstruation from the sterility clinic of the Women's Hospital. This paper will be presented at a future (post-war) date.

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THE RH FACTOR AND ITS APPLICATION TO OBSTETRIC PRACTICE.

By G. SHEDDEN ADAM, F.R.C.S. (Edinburgh), M.R.C.O.G.,
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UNTOWARD reactions following the transfusion of blood to post-partum and puerperal patients with evidence of intravascular hæmolysis, icterus and suppression of urine have received considerable attention recently, especially as these reactions have occurred after transfusions given under the most favourable conditions and after apparent compatibility had been established by the usual methods of blood typing and cross-matching.

The direct test between the recipient's serum and the red cells which are to be transfused will, in most cases, disclose any incompatibility; but an unsuspected antigen in the donor cells may be missed if the corresponding antibody is present in only small amount in the recipient's serum. If the direct test also includes a mixture of the donor's serum and the recipient's cells, its efficiency as a check will be enhanced.

Recent work[1] has shown that immune bodies to a variety of agglutinogens in transfused blood may be formed in a proportion of recipients who lack that particular antigen, so that a later transfusion of blood containing this antigen may lead to a severe or even fatal reaction.

A cause of incompatibility reactions of especial importance in obstetric practice is the Rh property recently discovered in human blood by Landsteiner and Wiener.[1] [2] Persons whose red cells contain an Rh binding substance or agglutinogen are said to be "Rh positive", and those whose red cells do not possess this antigen are said to be "Rh negative".

Levine[3] demonstrated that 85% of 1,035 persons were "Rh positive" and 15% "Rh negative". Antibodies (agglutinins) for the Rh factor do not normally occur in human plasma, so that when an "Rh negative" subject is given blood from an "Rh positive" donor as a first transfusion, the reaction may be absent or slight; but Rh antibodies are nevertheless produced, so that a second transfusion from an "Rh positive" donor may be followed by a fatal reaction.

In obstetric practice, however, it has been noted that it is not necessary for a woman to be given a second transfusion before incompatibility reactions involving the Rh factor can occur. The observation was made that most of the puerperal patients who had suffered transfusion reactions had been given blood from their husbands. Analysis of several of these cases demonstrated that the recipient was "Rh negative" and had moreover anti-Rh agglutinin in her serum, and that the husband donor was

[1] These authors used the immune serum of rabbits prepared by injection of the blood of rhesus (Rh) monkeys to detect the factor.

"Rh positive". The possibility was suggested[4] that the antibodies have been formed in response to an antigen present in the fœtus and inherited from the father, but absent in the mother. The concept of iso-immunization in the human body by the Rh factor was thus developed. These considerations have thrown new light on the ætiology of *erythroblastosis fœtalis*, which it is suggested results from the passage of the mother's anti-Rh agglutinins through the placenta to act on the susceptible red blood corpuscles of the fœtus.

Support for this contention is gained in the constant findings[5] that in cases of *erythroblastosis fœtalis* the mother was "Rh negative" and often had anti-Rh agglutinins in her serum, that the father was "Rh positive" and that the infant was "Rh positive". Intravascular hæmolysis in the fœtus with obstruction of the collecting tubules of the fœtal kidney, together with defective excretion through the placenta, would possibly account for the gross œdema so characteristic of the child with *hydrops fœtalis* (the œdematous form of *erythroblastosis fœtalis*). The overgrowth of the placental tissue may be a compensatory phenomenon, and the presence of immature erythrocytes in the blood film may well represent the strenuous efforts of the fœtal hæmopoietic centres to overcome the constant destruction of the more mature cells by hæmolysis.

It is probable that, in so far as the blood picture is concerned, a similar or related ætiology underlies the syndrome of *icterus gravis neonatorum*, which in fact may be considered as the non-œdematous form of *erythroblastosis fœtalis*. It is not uncommon for the two conditions to occur in infants born of the same mother (*vide infra*).

What, then, is the practical application of this new and important work to obstetric practice? In the light of our present knowledge, the matter appears to have a distinct bearing on (*a*) the giving of a transfusion of whole blood to puerperal and post-abortion patients generally, (*b*) the giving of a blood transfusion to puerperal patients who have given birth to an infant suffering from *erythroblastosis fœtalis* or one who within a day or two develops definite signs of *icterus gravis neonatorum*, (*c*) the giving of a blood transfusion to infants suffering from *icterus gravis neonatorum*. These points will be considered in greater detail with reference to relevant case records.

Blood Transfusion and Puerperal and Post-Abortion Patients.

If a blood transfusion is required for a woman during her pregnancy or puerperium, it is best not to use the husband as the donor, even though he is of the same blood group or a universal donor.[6]

It is apparently possible that some degree of iso-immunization may develop without producing signs of erythroblastosis in the infant, but sufficient to produce anti-Rh agglutinins in the mother's serum. If it is proposed to use the husband as the donor, the most careful typing and cross-matching must be carried out. It would be safer to look for compatible donors amongst the patient's blood relations (who are more likely to be "Rh negative", since this property is inherited as a simple Mendelian dominant). The difficulty, of course, could be overcome by testing the husband's blood, if it is otherwise suitable, against known anti-Rh serum as described later.

Blood Transfusion and a Previous History of an Affected Infant.

If a woman has given birth to an infant suffering from *erythroblastosis fœtalis* and requires a blood transfusion, in no circumstances must the husband be used as the donor, as he is almost certain to be "Rh positive" and the mother will be "Rh negative"; her serum will contain Rh antibodies, and a severe or even fatal reaction will follow. It would be as well to apply this rule also to mothers whose infants showed unmistakable evidence of *icterus gravis neonatorum*. In such cases, blood transfusions of whole blood may still be given, but only from a known "Rh negative" donor, and the technique for the identification of such donors is rapidly developing.

Serum from mothers who have recently been delivered of infants suffering from *erythroblastosis fœtalis* or *icterus gravis neonatorum* is often found to contain potent anti-Rh agglutinins. Samples of such serum should be stored in pathology departments attached to maternity hospitals. By its use in the circumstances described, the "Rh positive" donor can be eliminated with certainty. Group O blood reserved in blood banks for obstetric cases should also be tested against anti-Rh serum before being used for this purpose. The technique, which is relatively simple, is described by Mollison and Taylor.[6]

The immediate need is to build up stocks of serum containing the anti-Rh factor. If this is done, the fear of severe reactions following the giving of blood transfusions to puerperal patients generally, and to those patients specified above in particular, will be greatly diminished.

The following case record illustrates the type of reaction encountered.

Mrs. M.R. was pregnant for the fifth time and was aged twenty-nine years. Her first three pregnancies and confinements had been apparently normal. Her fourth pregnancy had terminated some two and a half years previously in the delivery of a stillborn fœtus whose body was said to have been greatly swollen; in view of subsequent events, it was almost certainly affected with *hydrops fœtalis*.

On September 25, 1939, at the Brisbane Women's Hospital, she gave birth to a stillborn, macerated fœtus, which manifested the ascites and generalized œdema so characteristic of this form of *erythroblastosis fœtalis*. The bulky, hyperplastic placenta helped to confirm the diagnosis.

A pronounced hypochromic anæmia had been present during the later weeks of her pregnancy; on September 21, 1939, the erythrocytes numbered 2,530,000 per cubic millimetre, and the hæmoglobin value was estimated as 30% of normal.

Although no post-partum hæmorrhage occurred at this confinement, it was decided that the patient's convalescence would be hastened and general condition improved by a blood transfusion during the puerperium.

On September 28 the blood groups of the patient and her husband were investigated, and both were found to belong to Group O. On September 30 six hundred cubic centimetres of citrated blood were given into the cubital vein by the indirect method, the donor being the husband. A rise of temperature to 102° F. followed within a few hours of the transfusion and some degree of icterus was noted later in the day.

On October 1, the following day, the patient was deeply jaundiced and complained of pain in the chest. Catheterization produced only half a fluid ounce of urine, which was acid in reaction and blood-stained.

It has been shown by Baker[7] that post-transfusional urinary suppression is due, at least in part, to the excretion of hæmoglobin (following the intravascular hæmolysis) with urine of high acidity and salt concentration. Under these conditions, the excreted hæmoglobin is converted to a granular deposit of hæmatin, which obstructs the renal tubules. It has also been demonstrated that, conversely, if the urine is constantly alkaline, no hæmatin granules are formed.

Efforts were therefore made to render the urine alkaline as quickly as possible; 170 cubic centimetres of Parke, Davis's "Alkaline Compound" were given intravenously, and an alkaline mixture was given by mouth every two hours.

The intravenous administration of alkali was followed by that of 400 cubic centimetres of a 12·5% glucose solution for its diuretic effect following the temporary elevation of the blood sugar level.

In an endeavour to ascertain the cause of the reaction, both the patient's and the donor's blood was retyped and cross-matched; but no agglutination could be detected after the patient's serum and the donor's red cells had stood in the incubator for fifty minutes. This can now be explained by the fact that the donor's cells would have temporarily absorbed most of the patient's serum agglutinins.[8]

On October 2 the patient's condition was much the same; the jaundice was still present, and the urinary output was only six fluid drachms for the twenty-four hours. During the afternoon, 500 cubic centimetres of a 25% glucose solution were given intravenously.

On October 3 the jaundice was less intense and the urinary output was four fluid ounces, the urine containing a heavy cloud of albumin. The urine was now alkaline. A blood count revealed 2,300,000 red cells per cubic millimetre and a hæmoglobin value of 27%.

On October 4 seven fluid ounces of urine were secreted, and on subsequent days the twenty-four hours' output expressed in fluid ounces was as follows: first day, 6; second day, 22; third day, 60; fourth day, 43; fifth day, 52; sixth day, 75; seventh day, 107.

The jaundice had disappeared by the end of the first week after the transfusion, and the blood count gradually improved with iron therapy.

As one looks back on this case, it is obvious now that an occurrence which some three years ago could be described only as an unexplained severe transfusion reaction, was in reality a case of incompatibility involving the Rh factor.

Blood Transfusion in Icterus Gravis Neonatorum.

The grossly œdematous subjects of erythroblastosis (*hydrops fœtalis*) are usually stillborn; only the less severely affected are likely to survive and therefore to require blood transfusion. Infants, however, exhibiting the related syndrome of *icterus gravis neonatorum*, are frequently given repeated blood transfusions in order to combat the progressive anæmia.

Since the blood of these babies is almost certainly "Rh positive", the mother's blood should obviously not be used, for her serum, which contains the Rh antibody, will only destroy more of the infant's red cells and aggravate the condition. Moreover, since the antibody has passed from the mother's serum to the blood of the fœtus *in utero*, the latter now contains these agglutinins as well; in fact, as has been previously suggested, this may be the explanation of the excessive intravascular hæmolysis suffered by these babies (who are "Rh positive").

The father, therefore, is not a suitable donor, for his red cells would be destroyed by the presence of the Rh antibody (acquired from the mother) in the infant's serum.

The most suitable donor is obviously one whose blood is "Rh negative" and whose serum does not contain the Rh antibody. If facilities for identifying the proposed donor as "Rh negative" are not available, the best line of action again would be to use one of the mother's blood relations, who are more likely to be "Rh negative" than an unrelated donor (since approximately 85% of donors are "Rh positive"). It is still necessary, of course, to exclude the possibility of choosing an "Rh negative" donor whose serum contained Rh antibodies. But these agglutinins do not normally occur in human serum; they appear to be present only after a transfusion of "Rh positive" blood has been given to a susceptible patient, and following iso-immunization during pregnancy as previously described.

By the exclusion of donors who have recently been given a blood transfusion, or who are pregnant or puerperal, the possibility that the transfused blood will contain Rh antibodies may be eliminated.

It is probable that, by the observation of these logical restrictions on the choice of a donor, the results of giving transfusions to babies with *icterus gravis neonatorum*—often previously unavailing—will be more successful and gratifying. A tragic feature in the past has been the tendency to recurrence of these abnormalities in successive pregnancies, possibly interspersed with the birth of a stillborn infant suffering from *hydrops fœtalis*. The following case records illustrate this point.

Mrs. L.W. gave birth to normal, full-term infants in 1929, 1931 and 1933. In 1935 she was delivered of a stillborn infant which was said to suffer from "dropsy". In May, 1941, she gave birth at the Brisbane Women's Hospital to a stillborn infant weighing nine pounds ten ounces and exhibiting the classical signs of *erythroblastosis fœtalis*.

On May 13, 1942, she was delivered of a living female infant weighing six pounds five ounces. On May 15 the child was deeply jaundiced, and the hæmoglobin value was 107%. Cross-matching tests with the mother's blood revealed no incompatibility, and the infant was given a transfusion the same day (60 cubic centimetres of citrated maternal blood into the saphenous vein). The following day the jaundice was, if anything, deeper; the hæmoglobin value was 100%, and death occurred on the fourth day.

Mrs. M.M. gave birth to a normal, full-term infant in 1938. In 1940 she was delivered of a living infant which, however, rapidly became jaundiced and survived for two days only. In February, 1941, she ceased to feel fœtal movements after thirty-six weeks' gestation, and subsequently gave birth to a stillborn infant showing all the signs of *erythroblastosis fœtalis*.

The patient was most anxious for another child, and in November, 1941, she presented herself at the Brisbane Women's Hospital, being then two months pregnant. She was delivered on June 15, 1942, of a grossly erythroblastotic infant, which survived for two hours. Her disappointment may well be imagined.

Discussion.

Since it has been customary in the past to use either the father or mother as donor, it is not inconceivable that a new hope may be offered to mothers such as these if the application of our knowledge of the Rh factor fulfils expectations, and further reports on this subject may be awaited with interest.

But, whilst a reduced mortality from *icterus gravis neonatorum* is in sight, the same cannot be said for the œdematous form of *erythroblastosis fœtalis*. The only application of our present knowledge towards its prevention would appear to lie in the pre-marital determination of the Rh character of the blood of the two persons concerned. It is doubtful, however, whether our knowledge of the subject is yet sufficiently full to enable us to advise against marriage when the indications (as shown by the Rh factor) are unfavourable.

It would seem that the potency of the Rh antibodies developed through iso-immunization during the first pregnancy may not be sufficient to interfere with the birth of a healthy child on this occasion, but that the risk of erythroblastosis or of *icterus gravis neonatorum* increases with successive pregnancies, especially if the interval between them is short.

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Addendum.

Since this article was written a bank of known Rh-negative blood has been established at the Brisbane Women's Hospital, and has been used with apparently successful results in recent cases of *icterus gravis neonatorum*. Repeated transfusions, however, are necessary.

SOME REMARKS ON HEAD INJURIES.[1]

By J. Estcourt Hughes, M.S. (Adelaide), F.R.A.C.S.,

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When it was arranged that my contribution to this programme should deal with head injuries, I was in some doubt as to whether I should make a brief general survey of the subject or select some particular aspect of the question and deal with it more fully. Even a casual survey of recent contributions to the subject of cranio-

[1] A post-graduate lecture delivered at Sydney on August 17, 1942, under the auspices of the New South Wales Post-Graduate Committee in Medicine.

cerebral trauma convinced me, however, that while there is complete agreement about the management of many types of head injury, in another group no such accord can be found, and that to weigh the pros and cons of any of these contentious matters would be impossible in the time at my disposal and would perhaps be of no considerable practical value in the end. With your permission, therefore, I shall outline the contents of some recent articles and indicate where material disagreements exist between the views expressed therein and those held by others. The classification of head injuries which we shall accept as a basis for our discussion is that which divides them into "open" and "closed" types with their respective subgroups.

From a London neurosurgical centre, O'Connell[1] has reported a series of 250 cases, in 148 of which the wounds were open and in 102 of which they were closed. He groups the open injuries into (i) scalp wounds, (ii) compound fractures, fissured or depressed, and (iii) wounds with cerebral penetration.

Scalp wounds are included in open wounds, because in this series and in series reported by others it was found that cerebral concussion, evidences of focal brain damage and changes in the cerebro-spinal fluid occurred in an appreciable proportion of scalp wounds. The association between infection of scalp and infective complications in the cranium and cranial contents is reemphasized, and a plea is made for the thorough *débridement* and exploration of even small scalp wounds.

In the discussion of compound fractures, the fundamental point is stressed that the crux of the matter is whether dural penetration has occurred or not, because the *dura mater* is the last barrier to the spread of infection to the brain tissue. O'Connell emphasizes the necessity for adequate treatment of depressed fractures. He points out that hair and other foreign material are often found between the bone and the *dura mater* and states that nothing short of the removal of the fragments and the thorough examination of the dura can be regarded as adequate treatment. He rightly condemns the method of making a trephine hole alongside the depressed area and levering up the depressed fragments from there, a process of "blind" elevation. In 37 cases of dural penetration cerebral hernia arose as a complication in eleven cases and cerebral abscess in four cases. In all the cases thus complicated recovery occurred, which is a most interesting result. The causes of the development of cerebral hernia are given as: (i) delay in instituting treatment, (ii) inadequate treatment and (iii) wide destruction of scalp, skull and brain. The methods of treatment which led to the highly satisfactory results, although the author does not go into details, were: (i) chemotherapy, (ii) posture, (iii) dehydration and (iv) lumbar puncture. The full recovery of the four patients with cerebral abscess was attributed to the facts that localization was easy, that in each case the abscess developed slowly and was therefore well walled off, and that tube drainage was possible through areas in which the meningeal spaces were obliterated by scarring and were therefore protected from contamination.

I should now like to turn from this interesting article to two other recent discussions dealing with war wounds of the head. One deals with injuries arising during the Western Desert campaign and the other comes from Hawaii. It has been widely accepted that casualties with head injuries travel relatively well, and that as a rule it is better in forward areas to carry out first-aid treatment only and then to pass head casualties back to a centre where a neurosurgical team with neurosurgical equipment is available. Captain Ackland's[2] instructions for first-aid treatment of head injuries are therefore noteworthy. After mentioning the disproportionately disastrous results of infection in head wounds, he recommends the following initial procedure to reduce the incidence of these complications. The wound should be gently opened and a gauze pad soaked in acriflavine placed in it. This is retained in position while a wide area of the surrounding scalp is clipped and shaved. The final shaving of the wound edges may be left until the operating centre is reached. Tincture of iodine is now applied to the shaven skin, the gauze pad is removed from the wound and sulphanilamide is sprinkled freely into the wound. A fresh acriflavine pack is inserted and retained by a bandage, or preferably by anchoring sutures through the skin edges.

This writer's further recommendations as to operative and post-operative measures follow standard lines; but I regret to note that he preaches one heresy, in that he can see no merit in practising two-layer scalp suture except in regions (for example, the forehead) where a better cosmetic result is thereby attained. My own feeling, and this is the orthodox view, is that the practice of approximating the *galea aponeurotica* with sutures of fine silk one-quarter of an inch apart and with the ends cut right into the knot and then suturing the skin, should never be replaced by the mere insertion of deep through-and-through sutures. The reasons for this two-layer method are: (i) accurate apposition of the aponeurotic layer on which the integrity of the wound depends is thereby ensured; (ii) superficial bleeding is more completely and more certainly controlled; (iii) the superficial layer of sutures can be removed much earlier when an efficient deeper layer is in place, the possibility of infection along the suture tracks being thus reduced.

In the article by R. B. Cloward[3] dealing with head injuries received during the bombing of Hawaii, of which I have seen only an abstract, there is substantial agreement with standard methods. However, he strongly advocates tight closure of any dural defects by the use of a strip of periosteum from the neighbouring skull, especially when a paranasal sinus is involved. This will prevent the development of a cerebro-spinal fluid fistula and will minimize the risk of infection. I think that this is over-stressing the importance of these fistulæ; most of them close spontaneously, and in any case their incidence after compound depressed fracture of the vault is uncommon compared with the incidence in fractures of the base of the skull, and early operation in the latter class has not been widely advocated. Cloward is in agreement with other recent writers in advocating the application of sulphanilamide locally and the use of chemotherapy by other available routes in open head injuries. In view of the fact that from cases of cerebral penetration arises a large proportion of the cases of post-traumatic epilepsy, Cloward advises for a year at least the use of adequate doses of an anti-convulsant drug, a suggestion which is worthy of full consideration and trial.

From the consideration of open head injuries we may now turn to the consideration of closed head injuries, and here one finds much less unanimity on the matter of treatment.

Sir Charters Symonds,[4] in a contribution to Brock's "Injuries to the Skull, Brain and Spinal Cord" which is the most important addition to the literature of craniocerebral trauma since Munro's book[5] appeared in 1938, outlines a scheme of treatment which I think should be regarded with general favour. He divides the care of a patient admitted to hospital in an unconscious state into three periods. Firstly, there is the initial period of thirty-six hours, during which associated injuries must be excluded or dealt with by suitable measures and during which shock must be treated. During this period constant clinical observation is necessary to determine improvement or retrogression in the patient's condition, and it is necessary to attend to fluid administration and the care of the bladder. If at the end of thirty-six hours the patient is still unconscious, but is quiet, lumbar puncture is performed, and if the pressure of the cerebro-spinal fluid exceeds 200 millimetres, fluid is allowed to run off until the pressure falls to 120 millimetres. Hereafter measures to lower intracranial pressure are the keynote of his treatment. These methods are: (i) daily lumbar puncture, (ii) elevation of the patient to Fowler's position, (iii) dehydration. Symonds decries the use of subtemporal decompression, but of this and of dehydration I shall have someting to say later. Blood-staining of the cerebro-spinal fluid Symonds regards as being an indication for repetition of lumbar puncture until the fluid is reasonably clear. For

restlessness the methods of treatment available are: (i) skilful nursing, (ii) the administration of 10 grains of potassium bromide and 20 grains of chloral hydrate in two drachms of water every four hours if necessary, (iii) the exhibition of morphine, and (iv) the giving of four drachms of paraldehyde at night. The third period of treatment commences when the patient has regained consciousness, and at this stage the therapeutic requisites are relief of headache, complete physical rest until giddiness and headache cease and a carefully graduated convalescence.

The *régime* briefly outlined above is one of active therapeusis, but it is well to remember that there is a school that believes in an attitude of masterly inactivity controlled by the strictest clinical supervision. In 1933 Dandy enunciated the tenets of this school, when he said that absolute rest was the most important aid that could be given to Nature's efforts to compensate for raised intracranial pressure, while careful and frequent bedside observation would disclose at all times the state of the intracranial pressure and would usually allow the surgeon to recognize and deal promptly with extradural hæmorrhage. Unless this condition was diagnosed, active intervention should be avoided unless Nature showed unequivocal signs of failure. In deprecating both lumbar puncture and dehydration, Dandy said that no patient had been saved by either.

The factors in a system of treatment, as suggested by Symonds, that have been criticized recently in various articles are: (i) the place of dehydration in treatment, (ii) the use of subtemporal decompression and (iii) the use of morphine as a sedative. Symonds himself admits that pulmonary œdema may follow the intravenous use of hypertonic solutions, and that an initial fall of intracranial pressure following the use of dehydration methods may be followed by a secondary rise to greater heights than the primary pressure.

Rowbotham[6] in his recent book summarizes the objections that have been advanced against dehydration as follows: (i) it may increase bleeding; (ii) it may interfere seriously with the general metabolic activities of the body; (iii) the tissues of the body may be over-dehydrated, with resulting toxæmia, the "toxic dehydration and acidosis" of Munro; (iv) lumbar puncture may be impossible in a restless patient, and in these cases it is wrong to induce dehydration on the assumption that pressure is raised; (v) there is no proof that cerebral œdema is an important factor in the production of symptoms in the early stages of trauma; (vi) theoretically it is inconsistent to bring about dehydration and to give fluids by mouth. The same author, however, makes a plea for consideration of subtemporal decompression in treatment. This advice coincides with that given by Dandy, that early and skilful subtemporal decompression will save a proportion of patients with acute head injury who would otherwise have died. Time will not allow argument on this subject, and I must be content to leave with you the thought that subtemporal decompression, even if its scope is limited, is not a dead operation.

Of the use of morphine in head injuries, Symonds states that morphine is sometimes necessary to control motor excitement, and that when employed judiciously for this purpose, it is harmless. He considers that by the time the higher centres have regained their functions sufficiently to allow coordinated movements of such a degree, the respiratory centre will be out of danger. The dose should be such as will produce a reasonable degree of calm, and it should not be repeated until the patient has had time to recover from its effect. In the United States of America there is opposition to the use of morphine as a sedative in head injuries, on the grounds that it masks symptoms, depresses respiration and causes a dangerous rise in intracranial pressure. Soluble phenobarbital is suggested as a substitute.

With this note I must close my fleeting survey of a small part of what has been written on head trauma since the outbreak of war, and I hope that, although nothing has been dealt with fully, some points of interest have emerged from the discussion.

Acknowledgement.

This paper has been submitted to the Director of the Naval Medical Service, Surgeon Captain W. J. Carr, C.B.E., R.A.N., and is published with his permission.

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Reports of Cases.

GRANULOCYTOPENIA COMPLICATING ADMINISTRATION OF SULPHONAMIDES: A REPORT OF TWO CASES.

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ALTHOUGH the occurrence of granulocytopenia during the course of therapy with various sulphonamides has already been recorded in the literature from many aspects, the cases described below present features which may be of interest. They are reported briefly with special emphasis on the points relevant to the discussion of the granulocytopenia.

Case I.

(F.C.)

On July 3, 1942, Corporal J.S.A., aged thirty-six years, was admitted to hospital under the care of Lieutenant-Colonel H. R. Love with a history of headache and vomiting extending over thirty hours. When examined he was drowsy and uncooperative, and no other details of his history were obtainable. He presented classical signs of cerebro-spinal meningitis. Meningococci were seen in a smear of his cerebro-spinal fluid and were also grown in culture. No organisms were grown on attempted culture from the blood after three days' incubation. He was given "M & B 693" twice a day, the dosage being twelve grammes on the first day, eight grammes on the second day, and subsequently six grammes per day. On the third day the free sulphapyridine in his blood was 3·0 milligrammes per 100 cubic centimetres and the total was 3·2 milligrammes per 100 cubic centimetres.

On the sixth day he was not showing the usual improvement; the mode of administration of "M & B 693" was changed to doses of one gramme every four hours. On the eighth day he developed a rash, and the administration of the drug was discontinued temporarily. At this stage his leucocytes numbered 9,000 per cubic millimetre of blood, 80% being polymorphonuclear cells. The sulphapyridine level in his blood was 2·4 free and 3·0 milligrammes total, per 100 cubic centimetres. His cerebro-spinal fluid was still turbid, and meningococci could still be grown on culture from it. On the eleventh day after his admission to hospital he began to show increased neck stiffness and his headaches were becoming more severe. Sulphapyridine therapy was recommenced with the administration of twelve grammes, eight grammes and six grammes successively on the next three days. On the thirteenth day, his leucocytes numbered 10,000 per cubic millimetre of blood. By the fifteenth day his condition was still the source of much worry, headache and neck stiffness still being severe. He was given five grammes of "Soluseptasine" intravenously.

On the seventeenth day the administration of sulphapyridine tablets was discontinued after a total of 99 grammes of sulphonamides had been given. He was given a mixture of potassium citrate and sodium bicarbonate in order to

alkalinize his urine. The leucocytes on this day numbered 8,000 per cubic millimetre. On the next day (eighteenth) the sulphonamide level in his blood was 2·5 milligrammes free and 3·0 milligrammes total, per 100 cubic centimetres, and the leucocytes numbered 13,900 per cubic millimetre.

His condition remained unchanged till the twenty-first day, and then became much worse; he was semi-conscious, incontinent of urine and fæces, and showing marked meningeal signs. Viable meningococci were still present in the cerebro-spinal fluid, which was opalescent. No organisms could be grown from the blood and the urine was clear microscopically; but the number of leucocytes had dropped to 1,700 per cubic millimetre, 24% being polymorphonuclear cells and 67% lymphocytes. The administration of "Pentnucleotide" was commenced, thirty cubic centimetres being given on this day and ten cubic centimetres on each of the following four days.

On the twenty-second day his condition was still extremely grave and was showing no improvement. On the twenty-third day the number of leucocytes had fallen to 1,000 per cubic millimetre, 5% being polymorphonuclear cells and 86% lymphocytes. At this stage he was noticed to have a right-sided hemiplegia, and bronchopneumonic signs appeared in his chest.

On the twenty-sixth day the number of leucocytes had fallen to 880 per cubic millimetre and a large bed sore appeared on his buttock. It was difficult to examine the patient's mouth; but there appeared to be some ulceration there. The dosage of "Pentnucleotide" was increased again to 30 cubic centimetres, and on the following day 40 cubic centimetres were given. The number of leucocytes after seven days of "Pentnucleotide" therapy rose to 8,000 per cubic millimetre, and on the following day to 16,000 per cubic millimetre. On this day also, for the first time, his temperature, which had been swinging from 98° to 102° F. ever since his admission to hospital, fell to normal, and clinically his condition began to improve.

On the thirty-second day, although he was still incontinent of urine and fæces, the number of leucocytes had risen to 33,000 per cubic millimetre, and his bed sores, though still large, were looking a little better; at this time he was noticed to have a motor aphasia. From this stage improvement slowly progressed. The number of leucocytes over the next three weeks gradually fell to 9,300 per cubic millimetre.

Comment.

It is now four months since his close brush with death; meantime he has shown a gradual but continued improvement, and though his speech is not yet back to normal, he can satisfactorily manage reasonably long sentences. Physical and occupational therapy have taught him to walk without obvious defect, and he has a well-controlled use of his right arm, though there is some limitation of movements, particularly at the shoulder.

Case II.

(J.J.H.)

Private R.V.A., aged twenty-three years, was admitted to hospital under the care of Major F. Blois Lawton on July 31, 1942. His illness had commenced seven days previously with shivering, followed by a cough, daily epistaxis and fever.

On his admission to hospital, his temperature was 101° F., his pulse rate was 120 per minute, his respirations numbered 30 per minute, and there were signs of pneumonitis at the base of the right lung. No other abnormal findings were revealed by physical examination.

He was given sulphapyridine, five grammes in all, on July 31, four grammes on August 1 and on August 2, and one gramme on August 3, a total of fourteen grammes during this period. In spite of this treatment there was extension of the inflammatory process involving both lungs, although his fever gradually subsided and there appeared to be a general improvement.

On August 7 his temperature began to rise again, and on August 10 a rash appeared, which lasted for about three days. It was regarded at first as possibly morbilliform, but later became more uniformly erythematous. As some enlarged glands were present in the posterior cervical triangle, the possibility of rubella was considered. On August 11, as the temperature had been 101° F. for two days past, and as widespread râles and rhonchi were present, sulphapyridine therapy was reinstituted, four grammes being given during the day. Some vomiting occurred, a small area of exudate was present on the left tonsil, and the evening temperature was 104° F. On August 12 further vomiting occurred. Sulphathiazole was given instead of sulphapyridine, and its administration was continued till August 18, four grammes being given each day (twenty grammes in all).

On August 13 the spleen was palpable. Cultural examination of blood and fæces was advised by Major Lawton; these investigations revealed no abnormalities. On August 14 the temperature fell to normal, and the patient felt well; but the temperature began to rise again on August 15. Chest signs indicative of pneumonitis were still present; but at this time, as throughout the illness, there was no clear correlation between the rises of temperature and the extension of pulmonary involvement.

On August 17 Major Lawton, with the possibility of typhoid fever in view, recommended a leucocyte count. This was made on August 18 and revealed a total count of 1,600 leucocytes per cubic millimetre. Only very occasional granulocytes could be seen in the film. There was nothing abnormal in the appearance of the lymphocytes or monocytes. In view of this finding, ten cubic centimetres of "Pentnucleotide" were given on this day and on August 19. On August 20 the temperature was 103° F. and the patient complained of sore throat. There was exudate of follicular distribution on the tonsils. Examination of throat swabs revealed none of the more likely pathogens (hæmolytic streptococci, diphtheria bacilli or Vincent's organisms). There was also a large pustule on the right wrist. As the leucocytes still numbered only 1,500 per cubic millimetre, Major Lawton recommended a blood transfusion; 600 cubic centimetres of citrated blood were given.

On August 21 the leucocytes numbered 1,300 per cubic millimetre, less than 1% being granulocytes; two cubic centimetres of bone marrow extract[1] were given.

On August 22 the leucocytes still numbered 1,300 per cubic millimetre. The hæmoglobin value was 84% (11·8 grammes per 100 cubic centimetres) and the erythrocytes numbered 4,100,000 per cubic millimetre. Another injection of bone marrow extract (one cubic centimetre) was then given. On this day also the patient received four cubic centimetres of "Anahæmin" and ten milligrammes of vitamin B_1.

On August 23 the leucocytes numbered 1,500 per cubic millimetre, and on August 24 the first appreciable rise occurred; the total number was then 3,200 per cubic millimetre, 5% being neutrophile polymorphonuclear cells. On this day sternal puncture revealed a granulocytic hyperplasia, 73% of the nucleated cells being premyelocytes. This finding suggested that regeneration of leucocytes was taking place, and that, provided the cause of the granulocytopenia was not still operative, the outlook was good.

During this period of severe granulocytopenia (August 18 to August 24) the patient showed considerable toxæmia and prostration, and the temperature remained at the level of 102° to 104° F. A good prognosis based on the appearance of the sternal marrow was, however, borne out by the subsequent course of the illness, during which the number of leucocytes steadily rose to a peak of 27,000 per cubic millimetre with a subsequent return towards normal in both total and differential counts. (Details of blood and bone marrow cell counts are shown in Table I).

A discovery of interest was that on August 25 (nine days after cessation of administration of the drug) the sulphanilamide content of the blood was 2·7 milligrammes per 100 cubic centimetres (2·3% in the free form). On this day also it was noted that the neutrophile granulocytes still showed vacuolation, as they had done also in previous films, as well as gross irregularity in size and staining of their granules, appearances which are usually attributed to the effect of toxic agents. In subsequent films these changes rapidly became less, and they were almost absent from those examined on August 28.

From this time onwards, the patient's condition improved slowly, and apart from a period of four days (from September 23 to September 27), when there was mild pyrexia each evening for which no cause could be found, and a slight persistent tachycardia, he was sufficiently well to be discharged to a convalescent home on October 1.

Discussion.

It is well known that transient polymorphonuclear leucopenia of mild degree not uncommonly occurs in the course of therapy with drugs of the sulphonamide group. In the large majority of cases, this finding is associated with the curative action of the drug. For example, in a case of pneumonia, it may produce rapid abatement of the toxæmia together with a fall in temperature from, say, 104° to 97° F., and in the total number of leucocytes from 16,000 to 4,000 per cubic millimetre, with subsequent satisfactory convalescence.

We are still ignorant, however, of whether the greater fall in the number of leucocytes, which occurs in a small

TABLE I.

Total and Differential Leucocyte Counts in Case II.

Date.	Number of Leucocytes per Cubic Millimetre.	Types of Cells. (Percentage.)										
		Neutrophile Polymorphonuclear Cells.	Old Metamyelocytes ("Band" forms)	Young Metamyelocytes,	Myelocytes,	Premyelocytes.	Myeloblasts.	Eosinophile Cells.	Basophile Cells.	Monocytes.	Lymphocytes.	Other Cells.
18/8/42	1,600	1·0	—	—	—	—	—	—	—	—	—	—
19/8/42	1,500	1·0	—	—	—	—	—	—	—	—	—	—
20/8/42	1,500	1·0	—	—	—	—	—	—	—	—	—	—
21/8/42	1,300	1·0	—	—	—	—	—	—	—	—	—	—
22/8/42	(1) 1,300	—	—	—	—	—	—	—	—	—	—	—
	(2) 1,300	—	—	—	—	—	—	—	—	—	—	—
23/8/42	1,500	—	—	—	—	—	—	—	—	—	—	—
24/8/42	3,200	4·0	2·3	—	0·7	—	—	—	—	31·5	60·0	1·5
24/8/42	(Bone marrow)	1·0	1·5	4·0	3·5	73·0	5·0	0·5	—	2·0	9·5	2·0
25/8/42	4,500	22·0	12·0	—	—	—	—	—	1·0	31·0	34·0	—
26/8/42	9,200	34·0	9·0	2·5	1·0	4·0	—	—	—	27·0	21·0	1·5
27/8/42	17,400	45·0	6·0	4·7	4·7	8·0	—	—	0·3	20·3	13·0	—
28/8/42	25,000	55·6	4·4	3·6	1·6	2·4	—	—	0·4	23·2	8·8	—
31/8/42	24,000	56·0	3·6	3·6	3·6	5·2	—	—	—	13·6	14·4	—
2/9/42	27,000	—	—	—	—	—	—	—	—	—	—	—
14/9/42	14,600	64·0	5·0	—	—	—	—	1·0	—	6·0	24·0	—

percentage of cases to a level that is of unfavourable rather than favourable import to the patient, and which becomes associated with other distressing symptoms, is merely an accentuation of the foregoing process (analogous in some ways to the anaphylactic episodes which occasionally complicate immunization), or whether it is determined by other factors. If the latter is the case, early recognition of such factors may enable us to forestall severe granulocytopenia, or to prevent by prompt treatment its more serious consequences.

Frequently repeated leucocyte counts during therapy and for some days subsequently offer at present our best means of early recognition of the condition; but in hospitals or other institutions dealing with large numbers of patients undergoing sulphonamide therapy, this measure in its most efficient form may be beyond the bounds of practicability. Estimation of the sulphonamide content of the blood during the days following cessation of intake may reveal a lag in excretion, which possibly constitutes a potential source of danger.

The first case described in this paper illustrates this advisability of continuing leucocyte counts and possibly also estimation of the blood sulphonamide level after withdrawal of the drug. On the day (the eighteenth of the illness) after the last dose was given, the number of leucocytes was at the satisfactory level of 13,900 per cubic millimetre, and as during the next two days the patient's condition remained unchanged, there seemed no reason to repeat the count. In view of the severe relapse on the twenty-first day, however, another count was made; this revealed a total of 1,700 leucocytes per cubic millimetre and the presence of granulocytopenia. It is possible that the fall in the number of leucocytes had occurred suddenly at some time during the previous two days, and that it was the predisposing cause of the exacerbation in the meningeal symptoms. If this was so, even earlier treatment than that instituted, including perhaps also the administration of bone marrow and active eliminatory measures, might have lessened the severity of the relapse. It is noteworthy that no improvement was detected until the seventh day after commencement of "Pentnucleotide" therapy, in spite of the large doses given. The accepted opinion is that a response is usually obtained within four or five days.

The second case illustrates several other points. The total amount of sulphapyridine given during the first period of administration (four days) was 14 grammes. This is a much smaller amount than that usually considered to constitute the "danger zone" (that is, about 50 or 60 grammes), although cases have been reported in which amounts smaller than this have produced granulocytopenia (for example, 27 grammes in a case reported by Drevermann and Gardner[1]).

In spite of this small dosage in our case, it was probably unwise to recommence the administration of the drug after an interval of seven days without a preliminary leucocyte count, as reactions presumably due to previous sensitization have been reported following such readministration.[1] In our case, it is unfortunately not possible to state with certainty at what stage the granulocytopenia commenced. The available evidence, however, suggests that it did not occur early during the readministration and therefore was probably not due to sensitization induced by the first course of therapy. The second course, in fact, appeared during its third and fourth days to be producing clinical improvement. If, however, the possibility of sensitization is considered, it is interesting to speculate as to whether the reaction was caused by the small dose (four grammes) of sulphapyridine given on the first day of the second course, or whether previous administration of sulphapyridine could induce sensitivity to sulphathiazole, twenty grammes of which were given during the subsequent five days of the second course.

Following the apparent clinical improvement on the third and fourth days of this second course, there was a further relapse; this, as has been indicated in the description of the case, prompted further investigations, among which was the leucocyte count which unexpectedly revealed a severe granulocytopenia. Two days later, there was an exacerbation of a previously mild tonsillar infection. This was not of the ulcerative or necrotic type usually found in agranulocytosis. However, as none of the organisms usually associated with ulceration or inflammation in this region were present, it and possibly also the pustule on the wrist were presumably due to invasion by normally avirulent organisms of tissues rendered non-resistant by the absence of polymorphonuclear leucocytes. During this period the patient was more severely prostrated and toxæmic than at any previous stage of his illness, and all known therapeutic measures that offered any possibility of relief were instituted. It is therefore impossible to assess the part played by any one of them. Had the sternal puncture been performed before the commencement of this treatment, it might have given an indication of whether the bone marrow appeared capable of regeneration without such "aids", the exact value of any one of which is by no means firmly established. Nevertheless, unless there is convincing evidence that they are unnecessary, it is doubtful whether they should be withheld in the case of a desperately ill patient.

The finding of a persistence of sulphonamide in the blood to the extent of a total of 2·7 milligrammes per 100 cubic centimetres on the ninth day after the cessation of intake may be of importance. Most investigators have found that these drugs are usually entirely eliminated from the blood in a much shorter period. Such delayed excretion, therefore, may be a potential or actual cause, by virtue of cumulative or continued toxic action on the granulocytopoietic system, of granulocytopenia during the later stages of therapy or even after withdrawal of the drug. In this case, the "toxic" appearance of the granulocytes, which also persisted until about this time, provided confirmatory evidence that a harmful agent was still operative.

It would appear, therefore, that estimations of blood sulphonamide level together with leucocyte counts and examination of blood films, made at the end of a course of

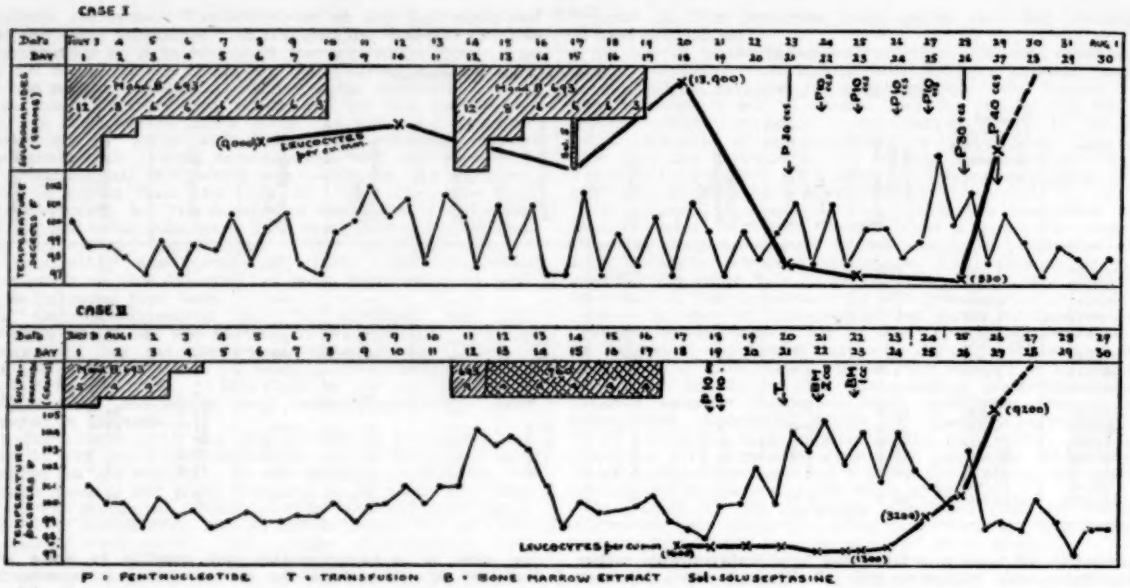

FIGURE I.

Charts showing temperature, sulphonamide dosage and other therapy and results of leucocyte counts.

sulphonamide therapy and once or twice during the subsequent week or so, would provide a warning signal. If facilities for estimation of the blood sulphonamide level are not available, and if the leucocyte count and careful examination of blood films for evidence of "toxic" appearances provide evidence of the persistence of the potentially toxic agent, it would seem that measures such as the administration of copious fluids to promote elimination as rapidly as possible should be undertaken.

The time relationships of the fever, drug administration and leucocyte counts in both cases are shown in Figure I.

Acknowledgements.

Major Lucy Bryce was responsible for the sternal puncture and other laboratory investigations in Case II, and for assistance and advice in the preparation of this paper. The blood counts in Case I were carried out by Captain Elsie Abrahams. We appreciate the generosity and helpful advice of Dr. Hilda Gardner, clinical pathologist to the Royal Melbourne Hospital, who supplied the bone marrow extract.

Major-General S. R. Burston, Director-General of Medical Services, has kindly given us permission to publish this paper.

Reference.

(1) E. B. Drevermann and H. J. Gardner: "The Schultz Syndrome (Granulocytopenia) with Special Reference to its Treatment with Extract of Yellow Bone Marrow", THE MEDICAL JOURNAL OF AUSTRALIA, June 22, 1940, page 851.

Reviews.

PRACTICAL MALARIA CONTROL.

"PRACTICAL MALARIA CONTROL", by an Australian, Carl E. M. Gunther, trained at the Sydney School of Public Health and Tropical Medicine, is, as its name implies, intensely practical.[1] All the carefully described methods have been worked out and found successful by him in the highly malarial environs of the gold mines in Papua.

He does not attempt to eliminate malaria, only to control it. This is at first sight disappointing, but when one remembers the wild country and the equally wild and scattered native population, one realizes that to eliminate malaria would be an impossibility at present, and, as the book goes to prove, would be disastrous. Papua cannot be compared with Malaya and still less with Panama. It is more like the undeveloped regions of Africa, where it was first realized that native races develop an immunity to malaria. The aim, therefore, should be to create a relative immunity in those Europeans who are likely to be exposed frequently to fresh infection.

The author has a very ingenious scheme for screening his non-immunes by placing a zone of animals and then of immunes, up wind, between the breeding grounds of the mosquitoes and the non-immunes. This may at first sight appear callous, but if the non-immunes become infected and are intimately associated with the immunes and the mosquitoes, they light up a virulent strain which attacks even the relatively immune natives.

The author's suggestions for personal protection, especially by skilled screening of houses and the use in the open of sensible clothing and of pyramid mosquito nets, are very wise, and he has even worked out a form of protection for the army in the field and in action, backed up by an energetic hygiene corps. He emphasizes that the *Anopheles* is a lover of twilight, for example, dark forests, dawn, sunset and moonlight. He gives a good summary of methods of dealing with mosquito larvæ and stresses the value of expert entomological advice in such cases, and the ease with which it can be obtained. Methods of collecting specimens and forwarding them will be found here in full detail.

The section on treatment is unorthodox, as no effort is made to eliminate the infection except in those who are leaving the country. Full doses of quinine if tolerated, or "Atebrin" if quinine is not tolerated, or a combination of both in old untreated infections, are given until the fever is under control, and then smaller doses are given for a few days longer, making a total dose of 200 grains of quinine. Thereafter prophylactic doses of quinine, five grains daily, may be taken so as to keep the infection subliminal and prevent reinfection. This, the author states, has no depressing effect.

The pathological and clinical sections contain full descriptions of a good staining method for malarial parasites, of the making of white cell counts, on the normality of which he lays great stress, and of tests for quinine in the urine. But he relies most on his clinical findings, and gives a clearly described unusual classification of these. There is a very full section on blackwater fever.

All army and other medical officers in the malarial districts north of Australia should have this book with them. It is small enough to slip into the pocket, and is a mine of information.

[1] "Practical Malaria Control", by Carl E. M. Gunther, M.D., B.S., D.T.M. (Sydney), with a foreword by Harvey Sutton, O.B.E., M.D., F.R.A.C.P., B.Sc., D.P.H., F.R.San.I.; 1942. Sydney: Consolidated Press, Limited. 7¼" × 5", pp. 91. Price: 6s. 6d.

The Medical Journal of Australia

SATURDAY, JUNE 5, 1943.

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HOOKWORM DISEASE.

ABOUT twenty years ago a great deal of work was done in Australia on hookworm disease. Anyone who cares to consult files of THE MEDICAL JOURNAL OF AUSTRALIA from 1918 to 1925 will find frequent reference to this common tropical disease—to the surveys made to determine its incidence, to the effect produced by it in affected human beings and to measures adopted for its eradication. Since those days a new generation of medical practitioners has grown up in Australia, who know but little of these investigations, and who, being seldom if ever faced with an affected patient, have no personal experience of the clinical manifestations of the disorder. At the present time men from every part of the Commonwealth are living and fighting in places where hookworm disease is endemic and where under the conditions of modern tropical warfare its prophylaxis is most difficult. Though the medical officers of the fighting forces will be fully instructed in the nature of the disease, its prevention and its early detection, infestations are certain to occur and it is quite likely that many of them will not be recognizable while the affected person is actually serving under front line conditions. It therefore is essential that civilian practitioners should know what to look for when infestation has occurred, should know what to do and should understand something of the magnitude of the task which eradication of the disease implies.

Hookworm disease, also known as ankylostomiasis, is caused by the hookworm *Ankylostoma duodenale* (from the Greek ἀγκύλος crooked or hooked, and στόμα a mouth) which is parasitic in the duodenum. It is a nematode worm, the male being about 10·0 to 12·0 millimetres in length and 0·4 millimetre in breadth, and the female slightly larger. The disease can also be caused by *Necator americanus* which is slightly shorter and more slender than *Ankylostoma duodenale*. Both types of worm have been found in natives of Papua and aborigines of Queensland.[1] The worm attaches itself to the mucous membrane of the duodenum and from this it sucks blood, giving rise to anæmia and causing mental and physical inertia. The eggs of the worm are passed in the fæces. In endemic areas in tropical countries sewerage systems are not found and the excreta are deposited in or on the soil. Here with the moisture and heat the larvæ develop and thrive. They enter the body of man through the skin of the feet and ankles and are conveyed to the intestinal tract. It is also held that the larvæ may be ingested with drinking water. From this short statement it is clear that on active service great care must be taken in regard to the disposal of excreta once infestation has occurred among the troops. As will be shown later, infestation does not at once produce signs or symptoms, and care in sanitary measures must thus be undertaken as though infestation were common. The use of a shallow latrine trench is not permitted; such trenches have been described as the ideal hatching ground for hookworm larvæ. The deep pit type of latrine is effective. Of course, the greatest danger arises from soil pollution by the native population, and this may nullify much of the effort put forward by the sanitary section of the army. Incidentally it should be stated that salt water is inimical to the growth of the larvæ; and it is notable that hookworm disease is not so prevalent in native villages in which the custom prevails of defæcating over the salt water of rivers and estuaries or over the open sea.

Before reference is made to the clinical aspect of the subject as it affects civilian medical practitioners, it is desirable that a short statement of the historical background of work in Australia should be made and that some indication of the magnitude of the problem should be given. As far as can be discovered, the first report of ankylostomiasis in Australia was made by J. B. Hogg, who in *The Australasian Medical Gazette* of February, 1889, reported a death from anæmia due to *Ankylostoma duodenale*.[2] This was followed in 1892 by the publication[3] in the *Transactions of the Intercolonial Medical Congress* (third session) of a paper by J. Lockhart Gibson and A. Jefferis Turner on the occurrence of *Ankylostoma duodenale* in Queensland. From then on occasional reports were published until in 1917 the first steps were taken towards an organized campaign against hookworm disease in Australia. From 1889 to 1917 inclusive it is stated[2] that 925 cases of hookworm disease were reported from all parts of Queensland. On the completion of its survey of Papua the International Health Board of the Rockefeller Foundation with the cooperation of the State Government commenced a survey of the State of Queensland. In October, 1919, the Australian Hookworm Campaign was initiated. This campaign was carried out under an agreement between the International Health Board of the Rockefeller Foundation, the Commonwealth Government and the Government of Queensland. The agreement covered a period of five years, and at the end of this time the Commonwealth took over the direction of the work. Some investigations in hookworm are still being carried out by the Health Department of the State of Queensland.

[1] W. A. Sawyer: "Hookworm in Australia", THE MEDICAL JOURNAL OF AUSTRALIA, February 19, 1921, page 148.
[2] Quoted by Sawyer, *loco citato*.
[3] J. H. Waite: "The Queensland Hookworm Campaign (First Progress Report Covering Period April 17 to December 1, 1918)", THE MEDICAL JOURNAL OF AUSTRALIA, December 21, 1918, page 505.

An indication of the extent of the work done in the early days of the campaign in Queensland may be gained from the first interim report covering a period of only seven and a half months.[3] The number of persons examined in Queensland districts was 14,577, and of these 21% were found to be infected. The Australian Hookworm Campaign did more than discover the number of persons affected. In the words of one of the medical officers of the campaign:[4]

> It has made contributions to our knowledge of endemiological factors, including the influence of rainfall, temperature, altitude, type of soil and factors favourable to the persistence of introduced local foci (as at the Goodna Hospital for the Insane) and also by intelligence tests (Binet-Simon and Porteus) has convincingly demonstrated that as a result of the anæmia and toxæmia produced and directly proportionate thereto mental retardation to the extent of two years has been caused by hookworm amongst many infected children.

Readers should perhaps be reminded that the Australian Hookworm Campaign was part of a world-wide investigation undertaken by the International Health Board of the Rockefeller Foundation.

In regard to the clinical side, it has recently been pointed out by Justin Andrews,[5] who writes from the Division of Malaria and Hookworm Service of the Georgia Department of Health, that adult hookworms suck blood continuously, and that the amount removed is proportional to the number of hookworms present. If they remove blood more rapidly than it can be formed, hookworm disease or anæmia results; if not, the condition is what Andrews calls subclinical hookworm infection. Since the chief objects of the present discussion, as already stated, are to bring to the notice of the civilian practitioner what he should look for in affected persons and what he should do for them, emphasis will be laid on this so-called subclinical state. Credit will undoubtedly be due to a practitioner who diagnoses hookworm disease in the presence of anæmia affecting a soldier freshly returned from an area where hookworm disease is endemic, for he will have to exclude anæmia due to such conditions as malaria, nutritional anæmia and sprue. He will make the diagnosis of hookworm disease by means of the levitation method, also called the saline or brine method, first described in 1921 by H. Hastings Willis[6] and universally adopted ever since. It cannot be too strongly insisted that the classical picture of anæmia is by no means always present. What generally happens is that the patient complains of indefinite, rather vague symptoms of discomfort in the epigastrium with feelings of tiredness and evidence of inertia; sometimes he does not feel well and cannot tell why. A patient complaining in this way will generally have an eosinophilia if he is harbouring an ankylostome or other worm and the careful application of the Willis test with the discovery of the ova on microscopic examination will settle the matter. The fact that the patient is seen in a non-epidemic area and the probability that the practitioner may have in mind only the classical sign of anæmia are quite likely to be misleading. In this connexion Andrews states some interesting views. He points out that hookworm disease is more likely to occur and will be more severe when infestation is high and iron-protein consumption by the patient is low. He thinks that when the amount of iron-protein consumption is adequate hookworm infection will with rare exceptions be subclinical, whether worm infestation is heavy or light. If these views are correct, and they are reasonable, then the practitioner must be more than ever on his guard when he discovers that the patient is taking and has been taking a well-balanced diet.

In the matter of treatment some changes have, as Andrews remarks, taken place in recent times. Carbon tetrachloride was the drug formerly used; it was effective, but not entirely free from risk. It has to a large extent been superseded by tetrachlorethylene. This drug is given with or without oil of chenopodium. The purpose of the drug is to destroy the adult worms. Whether this has been done can generally be determined by careful examination of the stools. It is important to remember that every worm killed represents a gain which cannot be reversed since the worms do not multiply in the body. Another observation, quite obvious, but easily overlooked, is the fact that anæmia in a person harbouring an ankylostome may not be entirely due to the worm. But we must forbear to enter upon the discussion of a subject so vast as the differential diagnosis of anæmia in such a case. What is really necessary is that the practitioner shall make it his business to be familiar with the different aspects of hookworm disease.

[4] H. R. Pearson: "Hookworm Disease and the General Practitioner", THE MEDICAL JOURNAL OF AUSTRALIA, March 28, 1925, page 314.

[5] Justin Andrews: "Modern Views on the Treatment and Prevention of Hookworm Disease", *Annals of Internal Medicine*, December, 1942.

[6] H. Hastings Willis: "A Simple Levitation Method for the Detection of Hookworm Ova", THE MEDICAL JOURNAL OF AUSTRALIA, October 29, 1921, page 375.

Current Comment.

HYPOGLYCÆMIC COMA.

THE increasing use of protamine zinc insulin for the management of diabetes and of induced hypoglycæmia for the treatment of certain mental disorders has, in recent years, stimulated interest in the cause of hypoglycæmic coma and death from it. R. D. Lawrence, A. Meyer and S. Nevin discuss the way in which the pathological changes found in the brains of patients dying in hypoglycæmic coma are produced.[1] Their study is based on the post-mortem findings in a series of cases of hypoglycæmic coma. The patients included diabetics, schizophrenics and one who suffered from an islet cell adenoma of the pancreas. Macroscopically no abnormality was seen in these brains except for some congestion which was not always present. Microscopic examination revealed widespread necrosis. The chief findings were loss of nerve cells, and the remaining cells showed homogenizing and ischæmic changes and also Nissl's severe cell changes. Microglial and macroglial proliferation was also present. These changes were found over wide areas of the cortex, in the caudate nucleus, the putamen, the basal ganglia and the cerebellum. This appearance suggests that the death of the nerve cells was brought about by a deprivation of oxygen. Similar or identical changes have been described in *status epilepticus*, "pertussis eclampsia", strangulation and in a case in which death occurred fourteen hours after an operation during the course of which the heart had stopped beating for ten minutes; and also after death from such anoxic poisons as carbon monoxide, cyanide and ether. Since it has been shown that the blood going to the brain and the venous blood leaving the brain is not deficient in utilizable oxygen in hypoglycæmia, these authors suggest that the anoxic changes in the nerve cells are due to their inability to utilize the oxygen. The high oxygen content of blood taken from the jugular vein during hypoglycæmic coma shows in fact that oxygen has not been used. The anoxic death of the brain cells is brought about

[1] *The Quarterly Journal of Medicine*, October, 1942.

by their chemical inability to utilize oxygen in the absence of glucose. Such mechanical interferences with the supply of oxygen as vasomotor disturbances, thrombosis or endothelial proliferation have been reported in post-mortem findings. These findings are not constant and therefore are not considered to be the main cause of the anoxia, but when present they would aggravate the disability of the brain cells. At first the changes in the nerve cells are reversible and a patient may recover completely from hypoglycæmic coma. With more prolonged coma the changes become irreversible and the patient persists in coma till death, even though adequate treatment may raise the blood sugar to normal levels for some hours or even days before death. This is illustrated by one of the cases reported by Lawrence. The patient in this instance could not have been in coma longer than ten hours before treatment started. Treatment brought the blood sugar to a satisfactory level and maintained it there for the next seventeen days when the patient died without ever coming out of the coma.

From the point of view of both prognosis and treatment the length of time for which coma has persisted is more important than the depth of coma. Deep coma and convulsions indicate a dangerous degree of hypoglycæmia, but prompt treatment can terminate the coma. It is the coma, even a light one, which has persisted for a few hours that is serious. It is impossible to state a definite time after which the cell changes become irreversible. Different individuals vary in the length of time during which they can be in coma and still recover; but coma that has lasted three hours or so has a grave prognosis. It is also obvious from the microscopic appearances that individual brain cells differ in their ability to withstand hypoglycæmia before irreversible changes take place. As was pointed out in a recent paper by W. S. Dawson and O. Latham published in this journal, it is probable that at least some brain cells are irreversibly damaged even though the patient recovers from a coma. Indeed the beneficial effect of convulsant therapy in mental disorders has been attributed by some authorities to this permanent damage. One would expect then that patients who have already experienced hypoglycæmic coma would have a lessened ability to withstand further attacks. This is borne out by a study of the case histories reported in the first paper mentioned.

METABOLISM OF A PARAFFIN.

IT has for long been regarded as axiomatic that a paraffin cannot be absorbed from the animal intestine and that it is metabolically inert. The paraffins are saturated hydrocarbons and are remarkably resistant *in vitro* to oxidizing agents such as chromic acid, permanganates and fuming nitric acid, and further no agent has been discovered in the digestive apparatus or in the varied armamentarium of the liver capable of dealing with them. It was therefore somewhat of a surprise when H. J. Channon and his collaborators showed that hexadecane, $C_{16}H_{34}$, can be absorbed and be reduced in amount in the living body to such a degree that katabolic action must be assumed.[1] It is true that "Vaseline" or paraffin wax injected subcutaneously gradually disappears, but this was supposed to be due to piece-meal removal by phagocytes rather than by local oxidation or by a digestive process like that which accounts for the disintegration of a ligature of ordinary catgut.

It was inevitable that this problem should be attacked by the new method of the radio-active isotope, in this case hydrogen, and it would appear that the question of paraffin absorption and katabolism, as far as hexadecane in rats is concerned, has been settled. DeWitt Stettin in the department of biochemistry in the Columbia University gave hexadecane with tagged hydrogen to rats and confirmed Channon's contention that this paraffin is absorbed; further there is a subsequent liberation of tagged hydrogen into the body fluids and an accumulation of this tracer element in the fatty acids of the liver.[1] Part of the hexadecane was recovered unchanged from the fat and lipoid matter of the rats' bodies. The same investigator showed that two other substances with 16 carbon atoms in the molecule underwent a precisely similar absorption and metabolism, namely, cetyl alcohol, $C_{16}H_{33}OH$, and palmitic acid, $C_{15}H_{31}COOH$, the last-mentioned being quite understandable and conforming with established doctrine. That hexadecane should be capable of taking part in the complex processes of life might have been inferred from the fact, known fully fifty years ago, but not mentioned by any of these authors, that it is found in quite a number of plants. So far the demonstration of the ability of an animal to absorb a paraffin possesses an academic interest only, for when liquid paraffin is administered orally to the human being it is recovered from the fæces in a quantity which is tantamount to 100% of what was taken by the patient, and this fact Stettin admits.

[1] M. A. H. El Mahdi and H. J. Channon: "Absorption of n-hexadecane from Alimentary Tract of Rat", *The Journal of Biological Chemistry*, Volume XXVII, 1933, page 1487; H. J. Channon and J. Devine: "Absorption of n-hexadecane from Alimentary Tract of Cat", *ibidem*, Volume XXVIII, 1934, page 467.

ŒDEMA OF THE ARM FOLLOWING RADICAL MASTECTOMY.

FOLLOWING radical mastectomy the most important complication is, of course, recurrence of the malignant disease; next in importance is the development of œdema of the arm. Many attempts have been made to explain the development of this œdema, and the theories as to its ætiology include: (*a*) post-operative inflammation, (*b*) venous obstruction, (*c*) fibrosis following post-operative irradiation, (*d*) recurrence of the malignancy with obstruction in the axilla, and (*e*) the theory of Reinhoff that considerable fibrosis occurs to obliterate the dead space left in the axilla. These theories have been discussed by S. Standard,[2] who concludes that the weight of evidence is in favour of a lymphatic obstruction. Several operations have been described for the treatment of this troublesome condition, but without any great success. Prophylactic efforts are, of course, indicated to prevent its development or to lessen its severity. These include gentle and careful operative technique during mastectomy to minimize the tissue reaction. Among other factors are the use of a minimal amount of non-irritating suture material, the attainment of asepsis, and the preservation of venous channels as far as possible. Reinhoff has suggested that in addition to these, a flap of the *latissimus dorsi* muscle should be swung across to fill in the dead space left when the flaps are tented over the axilla. This is held to reduce the amount of scarring and to provide an alternative route for lymph flow. This may be true in the early stages, but the non-functioning portion of the muscle in the axilla would soon atrophy and eventually become replaced by fibrous tissue causing further impairment of the lymphatic and venous flow. If these procedures fail, the problem may be approached in several ways. Non-surgical methods such as elevation of the arm followed by wearing of an elastic bandage about the arm provide some relief. Of the operations recommended amputation is the method of choice when severe pain is present and the heavy limb is useless. In other cases Kondeleon's operation of removal of portions of the deep fascia or the operation of lymphangioplasty may be tried, but only too often is the relief after operation transient. For such cases Standard has described an operation related to Reinhoff's procedure. He anastomoses the upper part of the inner side of the arm to the chest wall. After this operation the hand is still quite useful, and it is said that the augmented lymphatic or venous flow is followed by a reduction of the œdema of the arm. This procedure seems to be worthy of trial when amputation of the arm is intended. Amputation could still be performed later.

[1] DeWitt Stettin, junior: "Metabolism of a Paraffin", *The Journal of Biological Chemistry*, February, 1943, page 327.
[2] *Annals of Surgery*, December, 1942.

Abstracts from Medical Literature.

THERAPEUTICS.

Duodenal Ulcer.

H. SHAY, J. GERSHON-COHEN, S. S. FELS AND H. SIPLET (*The Journal of the American Medical Association*, November 7, 1942) discuss the physiological basis for diet therapy in duodenal ulcer. Milk and cream are effective because they are non-irritating, and call forth little gastric secretion compared with meat. Milk and cream also have an action on the disordered gastric function. Hypermotility, hyperperistalsis, hypertonicity and hypersecretion are characteristic of duodenal ulcer. Milk has a high acid-combining power. In a normal person, if milk is substituted for water in a water-barium meal, the gastric evacuation will be greatly prolonged, and this prolongation is still more marked when cream is used. Fat also has a similar effect. Gastric peristalsis and tonus are also diminished in this way, the mechanism responsible being in the upper part of the small intestine. This acid is neutralized for a long period and tonus and peristalsis are reduced by milk, cream and fat. Milk reduces gastric acidity more effectively the higher its fat content. This fat acts on a mechanism in the duodenum which causes a depression in gastric secretion. Other substances which activate this mechanism are gastric hydrochloric acid, dextrose, sodium chloride and bicarbonate. Cream is more effective than milk in reducing gastric acid. Olive oil stimulates the duodenum so that its function of controlling gastric motor and secretory functions becomes active. The addition of a small dose of olive oil fifteen to thirty minutes before meals, inhibits gastric secretion in patients with duodenal ulcer, and when it is tolerated is a sound addition to the diet.

Dark Adaptation.

V. P. FLYNN (*The Journal of Aviation Medicine*, September, 1942) describes a clinical test for dark adaptation. Five hundred fair pilots were tested. Each subject had to look at a bright light (two bulbs of 5,400 millilamberts each) for three minutes, then he was placed in a dark room 18 inches from a test light of 0·004 millilambert, and while looking a little above or below the light was asked to state when he could see the light. The average time taken was 60 seconds. Thirty-two pilots took over five minutes to see the faint light; some took only fifteen seconds. Those who took five minutes or more were treated with 10,000 units of vitamin *A* thrice daily for fourteen days. They were then retested and all were found to give results within normal limits. The rationale of the test is, that by looking at a bright light, the visual purple is exhausted, and the later appreciation of a faint light indicates the ability of the retina to regenerate the visual purple.

Sulphonamide.

T. N. HARRIS, H. E. SOMMER AND C. E. CHAPPLE (*The American Journal of the Medical Sciences*, January, 1943) describe administration of sulphonamide microcrystals by inhalation. These microcrystals can be suspended in aqueous solutions and injected. In the experiments referred to, however, a 5% suspension of sulphathiazole microcrystals was sprayed by an atomizer in a chamber containing white mice which were left in the vapour for fifteen minutes to four hours. The blood content of sulphathiazole was tested and found to vary between 1% and 16%. So little of the drug entered the stomach of the mice, that there was no doubt that absorption of the drug was due to inhalation of microcrystals. Very low concentrations of the drug were found in the lungs after exposure, indicating that there was rapid solution in the blood stream on inhalation. This method was found to reduce greatly the mortality of mice infected with pneumococci.

Dicoumarin.

C. S. DAVIDSON AND H. MACDONALD (*The American Journal of the Medical Sciences*, January, 1943) discuss the action of 3-3-methylene-bis (4-hydroxycourmarin) or dicoumarin as a substitute for heparin. They found that the prothrombin concentration of the blood usually fell soon after the drug was given, but the fall was variable in time and quantity and it was not possible to predict the effect. Doses of one to two grammes were administered by mouth to eight selected patients, two of whom were essentially normal in health. The coagulation time of the blood after dicoumarin was given was extremely variable. These results were not affected by adequate doses of vitamin *K* or blood transfusion. The coagulation time of the blood was prolonged to a variable but not a marked degree by dicoumarin, but the effect was very difficult to control. Dicoumarin is not at present considered a good substitute for heparin.

Vitamin K.

J. G. ALLEN (*The American Journal of the Medical Sciences*, January, 1943) has described tests with a water-soluble vitamin *K*-like substance, tetrasodium-2-methyl-1, 4-naphthohydroquinone diphosphoric acid ester, or "Synkayvite" (Roche). This substance was given orally, intravenously or intramuscularly in doses of five to twenty milligrammes to patients who had a lowered prothrombin blood content due to inadequate absorption of vitamin *K* from the intestinal tract. The patients suffered from a variety of diseases mainly affecting the liver, such as carcinoma of the pancreas, biliary calculus, cirrhosis of the liver, stricture of the common duct and so on. The results indicated a rise in prothrombin level to normal in the majority of patients even where the level had been as low as 18% beforehand. This rise was noted within twenty-four hours and was still evident after seventy-two hours. To test the toxicity of the preparation, 200 milligrammes of the drug were given intravenously without ill effect to two different patients normal in health. The lower values for prothrombin were noted in common duct stone, carcinoma of the head of the pancreas, common duct stricture, and ulcerative colitis. In cirrhosis, large leuchæmic liver, secondary carcinoma of the liver and acute catarrhal jaundice the prothrombin level in the blood in this series of 48 cases was not markedly lowered.

Sulphathiazole in Epidemic Sonne Dysentery.

THE beneficial effects of sulphathiazole on the clinical course of endemic bacillary dysentery are well known, but there has been no information concerning the length of time elapsing before the dysentery bacillus can no longer be demonstrated in the stools and the incidence of relapses. Herman Yannet *et alii* (*The Journal of the American Medical Association*, September 19, 1942) present the findings in a small outbreak of Sonne dysentery in which data were obtained relating to these two points. It was hoped that the use of sulphathiazole would shorten the time of the carrier state and thus reduce the period of isolation. This did not prove to be the case and actually the organisms were demonstrated for much longer periods in the treated group than in the controls. This prolongation of the carrier state makes the problem of epidemic control much greater. It would appear therefore that the routine use of sulphathiazole in institutional epidemics is not desirable. Its use in selected cases, however, is of undoubted value. It was also determined that the bacteriostatic effect of the drug may mask the presence of the dysentery organism and positive cultures may be obtained as late as three weeks after cessation of therapy.

NEUROLOGY AND PSYCHIATRY.

Prefrontal Leucotomy.

FIFTEEN cases of mental disorder in which treatment by prefrontal leucotomy was used are presented by G. W. T. H. Fleming and Wylie McKissock (*The Lancet*, March 20, 1943). Reference is made to a modification of the surgical technique: the usual leucotome was not used, but was replaced by an ordinary ventricular trochar and needle, the latter being withdrawn to see if any cerebro-spinal fluid was escaping and the white matter divided by the blunt end of the trochar. Slight bleeding was occasioned in several cases, but otherwise there were no alarming surgical complications. The post-operative care is described in detail, and short case histories are given. There were no deaths. Of twelve melancholic patients, seven made good recoveries. One schizophrenic patient remained unimproved, but an obsessional neurotic is stated to have completely recovered. The manic-depressive patient showed some improvement.

Results of Prefrontal Leucotomy.

E. L. HUTTON (*The Lancet*, March 20, 1943) gives details of fifty psychotic patients treated by prefrontal leucotomy. Two patients died, but only one as the direct result of the operation. Otherwise the post-operative course appeared uneventful. In some cases there was transitory enuresis and an epileptiform attack was recorded

in one instance some time after treatment. On account of the radical nature of the treatment only patients with chronic conditions were treated, and then only after other methods of treatment had failed to bring about any beneficial change in the mental state. Taking this into consideration, the author finds the results encouraging. No patient was made worse by the treatment and many while not recovering were definitely benefited. The least successful cases were among the schizophrenic group in which apathy and emotional blunting had become obvious. The author notes that personal attention and encouragement in the post-operative period are very helpful in bringing about a satisfactory remission.

Social and Economic Factors in Psychiatry.

W. LINDESAY NEUSTATTER (*The Eugenics Review*, July, 1942) has studied poor economic conditions in relation to mental defect, psychoses and neuroses. Among the fifty poor families investigated, 35 had not enough money for the British Medical Association minimum dietary requirements, and 19 out of 20 of these had not the minimum caloric requirements, yet only 20% of the children were nervous compared to 38% of the well-to-do group, and the conclusion is drawn that poor social conditions are not in themselves a direct determinant of nervousness in children. Provided the psychological home situation is good, the author believes that bad social conditions have no adverse psychological effect on children. There was, according to this investigation, a definite relationship between nervous children and nervous parents, irrespective of economic factors. Though bad physique is commoner among the poorer classes of children, poverty, in the opinion of this author, is not enough to cause nervous symptoms.

Depression of Brain Metabolism in the Treatment of Schizophrenia.

BECAUSE biochemical analyses have disclosed that the shock treatments of schizophrenia subject the brain to metabolic depression, C. H. Bellinger, C. F. Terrence, B. Lipetz and H. E. Himwich (*The Psychiatric Quarterly*, January, 1943) investigated the effect of inhaling undiluted nitrogen as a means of depressing cerebral metabolism. The method had been previously described. The patients received forty treatments. The writers find that short periods of anoxia exert a favourable effect on the course of schizophrenia and that insulin, "Metrazol" and nitrogen inhalation produce depression of cerebral metabolism. The chief difference between these various forms of treatment is in the duration of the cerebral depression; and the authors believe that the higher recovery rate obtained by the use of insulin may be chiefly due to the more prolonged depression of brain metabolism.

Syndrome of Amyotrophic Lateral Sclerosis of Bulbar Type Associated with Platybasia.

RICHARD H. YOUNG (*The Journal of Nervous and Mental Disease*, February, 1943) reports two cases of amyotrophic lateral sclerosis of bulbar type in which a condition of platybasia was demonstrated by X-ray examination. The similarity of the clinical features in these two cases suggests that the platybasic deformity may play a role in the production of this type of illness, more especially as surgical decompression of the *foramen magnum* produced striking amelioration of the symptoms in one instance. The author contends that X-ray examination of the skull and upper cervical vertebræ together with lumbar puncture and the measurement of cerebro-spinal fluid pressure are desirable and may furnish valuable evidence in cases of amyotrophic lateral sclerosis; and he suggests that when there is evidence of platybasia, surgical decompression may give beneficial results.

Preliminary Curarization in Electric Convulsive Shock Therapy.

PAUL T. CASH AND CLARENCE S. HOEKSTRA (*The Psychiatric Quarterly*, January, 1943), seeking to safeguard patients from traumatic hazards associated with convulsion therapy, have experimented with the use of a preliminary injection of curare; and they report on its use in 139 cases in which patients were treated by means of electric convulsions. They believe that the electric shock method of inducing the convulsion is superior to the chemical method. In their opinion the traumatic effects of the treatment are not confined to fractures of the vertebræ or long bones, but may arise in the form of petechial hæmorrhages in certain viscera and may increase the incidence of tuberculosis. The dose of curare is estimated from the body weight, one milligramme being used for every two pounds. By preliminary curarization, treatment may be given in cases in which in the ordinary sense, convulsion therapy would be contra-indicated. The best results in this series were obtained in the depressive psychoses. One death due to electric shock is reported.

Schizophrenia in Cryptogenic Narcolepsy.

SAMUEL R. LEHRMAN AND EDWARD J. WEISS (*The Psychiatric Quarterly*, January, 1943), after reviewing the literature on narcolepsy, present a case of cryptogenic narcolepsy associated with paranoid schizophrenia. Such cases are apparently rare and the authors draw attention to the fact that the schizophrenic syndrome is always of the paranoid type. In the case presented the paranoid projections seemed to originate in the patient's self-consciousness over her narcoleptic attacks.

Group Psychotherapy for War Neuroses.

DONALD BLAIR (*The Lancet*, February, 1943), confronted with the problem, in his capacity of army psychiatrist, of treating successfully a large number of patients in a limited time, has resorted to the practice of group psychotherapy. After a preliminary interview with each individual patient, the patient was instructed to write his own history with special reference to events which were thought to have affected his mental welfare. Another long individual interview was given and then the patients went into class for ten lectures, on such subjects as fear, sex, self-treatment *et cetera*. The author considers his results encouraging. The group method was appreciated and after attending the lectures patients were found to be able to discuss their symptoms more intelligently and helpfully. The author's objective was to return as many men as possible to the forces in some useful capacity and to send the remainder back into civilian life capable of beginning useful work immediately. He considers that the objective was realized.

Diagnosis of Psychogenic Factors in Disease by Means of the Rorschach Method.

M. R. HARROWER-ERICKSON (*The Psychiatric Quarterly*, January, 1943) sets out to show that the suspicion that psychogenic factors may play an important part in a patient's condition may be confirmed by the Rorschach test. This it is claimed may prove very useful in differentiating those maladjusted patients whose physical conditions are mainly or entirely due to psychological factors.

MEDICINE.

Diabetes Mellitus.

ARTHUR R. COLWELL (*Archives of Internal Medicine*, October, 1942) discusses the observed course of *diabetes mellitus* and inferences concerning its origin and progress. An analysis of 166 cases of proved *diabetes mellitus* was made from three standpoints: first, the age at which the disease was recognized (age at onset); second, the length of time it was known to have existed up to the time of study (duration); and third, the daily dose of insulin necessary for satisfactory control of the disease (insulin dose). The age of these patients varied from six to eighty-two years. The author states that if the insulin dose is used as a gauge of the severity of the disease in groups of patients of different ages and at different stages of the disease, the following interpretations appear to be justified. Diabetes is inherent and begins at birth, and before it is recognized in clinical practice it progresses through a stage, the magnitude of which is fully as great as that of the known diabetes which follows recognition. Also, the rate of its progress is indicated by the age at which it is recognized; the earlier it appears, the more rapidly it progresses. It is probably more nearly correct to say that the more rapidly it progresses through its unrecognized stage, the earlier in life it appears. Further, the disease tends to improve temporarily during the first few years after its recognition, probably as a result of treatment, but this improvement does not affect its subsequent course. There are indications that after some ten years of known existence, the disease may show progressive and permanent improvement. These interpretations frequently appear to be violated in aged persons with diabetes, probably because of the presence of chronic complications.

British Medical Association News.

SCIENTIFIC.

A MEETING of the South Australian Branch of the British Medical Association was held at the Adelaide Children's Hospital on October 29, 1942, DR. R. J. VERCO, the President, in the chair. The meeting took the form of a number of clinical demonstrations by members of the honorary medical staff of the hospital.

Congenital Glaucoma and Congenital Heart Disease.

DR. HELEN MAYO showed an infant, aged eighteen months, suffering from congenital glaucoma and congenital heart disease. The mother had had German measles at the second month of gestation, and the infant at birth weighed only four pounds. Extreme difficulty in feeding the child was experienced in the first year of life, and she was restless and difficult to manage. At the time of the meeting she was less restless; she was small for her age and had had several operations to the eyes, and the "machinery" heart murmur and lack of cyanosis indicated a patent *ductus arteriosus*.

Dr. Mayo stressed the frequently serious congenital defects found in children of mothers who had suffered from German measles in the early months of pregnancy. The most frequent abnormalities were congenital cataract, congenital *morbus cordis* and mental deficiency. An investigation now being carried out at the Institute of Medical and Veterinary Science aimed at determining the percentage of defective children born to such mothers. If the incidence was high, termination of pregnancy might be justified.

Spasmus Nutans.

DR. CONSTANCE FINLAYSON showed a child, aged one year, suffering from *spasmus nutans* or head nodding with nystagmus, of nine weeks' duration. She presented the typical features of the condition, the nodding ceasing during sleep and becoming worse when she focused her eyes on an obect. When looking at anything she looked out of the corner of her eyes, and it was then seen that she had a nystagmus. Her sclerotics were bluer than normal; but otherwise her eyes were normal.

Dr. Finlayson said that the cause of this rare condition, which occurred during the winter months in children aged under two years, was unknown. Poor lighting of houses and rickets, the two suggested ætiological factors, were not present in the case under discussion; the mother lived in a satisfactory house and had given the child cod liver oil regularly. The prognosis was good, recovery taking place in weeks or months.

Encephalitis following Measles.

DR. M. E. CHINNER showed four children who had had encephalitis following measles. Two of the children had had the disease in the previous epidemic in 1940, and two had been affected in September, 1942.

The first patient, a girl, aged five and a half years, was in a mentally deficient state. She had developed encephalitis six days after the rash of measles appeared. She was unconscious and irritable, but showed no other neurological signs. At the time of the meeting, six weeks later, she was mute, totally blind and deaf, groped to find her surroundings and could just stand with support. She had trophic ulcers on her left hand, her left arm and the left side of her chest, but now felt pain when the ulcers were dressed.

The second child, a girl, aged six years, had had measles encephalitis of much the same type two years previously. She had been stuporose and apparently blind; but at the time of the meeting the only abnormality was some intention tremor on holding the hands outstretched and on putting finger to nose and heel to knee. Her gait was unsteady, but her speech was normal.

A third child, aged nine years, who had had constant head rolling movements, blindness and coarse tremor of the upper limbs at the onset of her illness at the end of 1939, passed through a stage of Parkinsonism in 1940 and 1941. During this time her face appeared expressionless, and tremor of the hands with some pill-rolling movement was present. She could move her lower limbs, but seldom did so. At the time of the meeting she was in splendid physical condition; she spoke slowly with a lisp and had difficulty in saying some words. There was a slight tremor of the hands, and she found it difficult to write on the line, though she was learning well at school. She walked with a little ataxia and some dragging of the toes. Her knee jerks were very active, but the plantar reflexes were flexor in type.

The fourth child, a boy, aged fifteen years, who had had encephalitis seven weeks previously, had exhibited few cerebral signs, but had shown signs of myelitis. His legs originally were affected by a flaccid paralysis, and he had retention of urine with overflow. The condition rapidly improved, and at the time of the meeting, seven weeks later, he was beginning to walk, though with some weakness of the right leg. The knee and ankle jerks were now present, but sluggish.

Dr. Chinner said that the ætiology of the condition was still obscure. It was not considered to be directly due to the measles virus, and therefore in treatment convalescent serum was no longer being given. It might be due to a change in the measles virus, by which it had become neurotropic in character. It might be due to a chemical change occurring during the course of the measles, which led to demyelination in the nervous system. The usually accepted explanation was that the measles activated another virus, neurotropic in type. The encephalitis was of the demyelinating type seen in disseminated sclerosis. In the same way that signs in disseminated sclerosis resolved, so might those of post-measles encephalitis. Dr. Chinner did not consider that mumps meningitis came into the same category; it was probably primarily due to a neurotropic virus which was excreted by various glandular tissues of the body. In this disease the prognosis was good. In measles encephalitis, of the patients that recovered, 65% showed some residual neurological disability.

Lung Consolidation.

DR. R. L. T. GRANT showed a boy, aged sixteen years, who had had an area of consolidation in the upper lobe of the right lung for one year. Cough with sputum had developed about a month after tonsillectomy. The diagnosis was in doubt. The long history did not suggest an abscess or the presence of a non-opaque foreign body, the absence of reaction to the Mantoux test excluded tuberculosis, and the absence of reaction to the Casoni test suggested that the condition was not a hydatid cyst. The boy's general condition had not deteriorated, and a fungous infection was therefore unlikely. A bronchogram had been unsatisfactory, as the contrast medium did not fill the bronchus to the affected area, and a bronchoscopic examination had been suggested.

DR. E. BRITTEN JONES said he thought a bronchoscopic examination should certainly be made, and suggested that the condition might be a tumour, though he would not like to say of what type.

Bronchiectasis Successfully Treated by Pneumonectomy.

DR. D. G. MCKAY showed a boy, aged nine years, who ten months previously had undergone pneumonectomy for bronchiectasis. The boy had a history of several hæmoptyses and attacks of pneumonia, once with an effusion. A bronchogram had revealed saccular bronchiectasis of the lower lobe and the lingular bronchus of the upper lobe of the left lung. A large cyst, which later could not be demonstrated by radiological examination after the injection of oil, appeared to be associated with the lingular bronchus. Artificial pneumothorax with the production of adhesions by the injection of silver nitrate into the pleural cavity prepared the child for the operation. It was found at operation that the lingular portion of the upper lobe could not easily be differentiated from the remainder of the lobe, and it was thought safer to remove the whole lung. The child did well after the operation; no effusion or empyema developed, and at the time of the meeting he looked exceedingly healthy. He could run and play with other boys of his own age, and according to his mother he was in better health than ever before. From the front, practically no flattening of the chest was visible; but the apex beat was in the left axilla. Posteriorly, a slight scoliosis was apparent, the left side of the chest was slightly flattened and the scapula was slightly winged.

Osteochondritis of the Hip Joint.

DR. WALLACE JOLLY showed two patients suffering from osteochondritis of the hip joint. The first was a girl, aged five years and seven months, who had had a congenital dislocation of the affected hip treated at the age of eighteen months. Reduction was difficult, two attempts being necessary. After removal of the last plaster cast one year later the child walked well, and subsequent skiagrams showed the position to be satisfactory. She was quite well until two

weeks before she attended the out-patient department on September 19, 1942, when she gave a history of pain in the left thigh and a limp. On examination, 15° of fixed flexion and gross limitation of internal and external rotation of the femur were noted. The radiologist reported the presence of fragmentation of the head of the femur and widening with *coxa vara* deformity of the neck; the appearances were typical of Perthes's disease.

Dr. Jolly said that the interest of the case lay in the fact that the possible cause of the osteochondritis was the trauma of reduction of the congenital dislocation of the hip. McMurray had stated that Perthes's disease commonly followed congenital dislocation of the hip; but that had not been Dr. Jolly's experience. The child was treated by Pugh's method of extension, and at the time of the meeting fixed flexion was much diminished.

Dr. Jolly's second patient was a girl, aged nine years and nine months, who on October 7, 1942, gave a history of pain in the hip and limping with the right leg, of three weeks' duration. She was not sleeping well. She walked with the hip abducted and slightly flexed. On examination, muscular wasting, 5° of fixed flexion, limitation of abduction and gross limitation of rotation were found. The Mantoux test failed to produce a reaction. The radiologist reported that there was no evidence of Perthes's disease, and that the condition was possibly osteochondritis of the acetabulum. The child was treated by Pugh's extension, and had many carious teeth extracted. Dr. Jolly considered that the condition was unlikely to be chronic osteochondritis on account of the way in which the active signs had quickly subsided. Dr. Jolly said that it was of interest to speculate why rotation was so much limited in this type of case.

Rickets Resistant to Treatment.

DR. MARGARET HORAN showed two children, of whom one was under the care of Dr. Britten Jones and the other under the care of Dr. Grant; the children were suffering from rickets resistant to ordinary curative doses of vitamin *D*. One patient was a boy, the other a girl; they were not related to each other. Both were aged four and a half years, and both had been under observation for between twelve and eighteen months. Both had been brought to the hospital on account of bowing of the legs; they had been given cod liver oil in average adequate dosage in the first eighteen months of life, and neither had been confined indoors. Neither had had any serious illnesses in infancy. Their physical appearance, except for skulls and teeth, was typical of florid rickets. X-ray films of the long bones confirmed the diagnosis; a general haziness of the bony trabeculæ, evidence of blurring of the epiphyseal line and increase in diameter of the epiphysis with some cupping were seen. These changes were more pronounced in the boy than in the girl, but were not so gross in either as the clinical appearance suggested.

Dr. Horan went on to say that the blood chemistry, though not fully confirmative, did not exclude rickets. The serum calcium level was always within normal limits. The serum phosphorus level ranged between 3·9 and 4·2 milligrammes *per centum* in the girl and in the boy it remained at 3·7 milligrammes *per centum*. Dr. Horan said that according to Park, of New York, a blood level of 4·0 milligrammes *per centum* of phosphorus was the dividing line below which rickets occurred. The phosphatase values were greatly raised; in the case of the boy the value was 74 units per 100 cubic centimetres of blood and in the case of the girl 55 units. In the case of the girl, cœliac and renal rickets were excluded by test meal examination, by fæcal examination, by urinary excretion tests and by excretion pyelography. No test meal examination was made in the case of the boy, nor was excretion pyelography carried out; but there was no clinical evidence of cœliac or renal rickets. Neither child showed evidence of liver insufficiency. The girl was given injections of 5,000 units of vitamin *D* per day for a week, then 5,000 units by mouth for three weeks; but no improvement followed. The boy was given the same dose by mouth. Over a period of fifteen months in the case of the girl and eight months in the case of the boy no improvement could be detected, the dosage of vitamin *D* being 5,000 units per day given by mouth. Dr. Horan said that in the literature cases similar to those under discussion were described as rickets resistant to ordinary doses of vitamin *D*, but responding to massive doses of from 150,000 to 1,500,000 units per day. The two children were given 150,000 units by mouth per day, and in three months radiological and serological improvement was apparent. The literature stated that it was possible to give too much vitamin *D*; but this could be avoided by regular examinations for hypercalcæmia and the presence of calcium casts in the urine. Dr. Horan said that it was reasonable to expect to encounter a greater number of cases of resistant rickets in Australia, where food and sunshine were abundant, than of cases of true infantile rickets.

A MEETING of the Victorian Branch of the British Medical Association was held on May 5, 1943, at the Royal Australasian College of Surgeons, Melbourne, DR. J. S. CAHILL, the President, in the chair.

The Work of the Australian Red Cross Society.

Dr. J. Newman Morris, C.M.G., Chairman of the Victorian Division of the Australian Red Cross Society, gave an address on the work of the society to an audience consisting of members of the Branch and their wives and officers of the Australian Red Cross Society and its Victorian Division. The audience was treated to a splendid account of Dr. Newman Morris's travels in the interest of the Australian Red Cross Society, covering 40,000 miles and occupying five months. In a most felicitous manner the lecturer intermingled personal experience of conditions existing for travellers in America, Africa and portions of the Continent of Europe, with observations on treatment and nutrition of prisoners of war in the hands of the Axis powers and comments on Red Cross organizations in many countries.

It was apparent to those present that Dr. Morris did not take them into his confidence concerning what must have been the most important portion of his work while abroad. He omitted all reference to the manifold benefits for the work in Australia which will follow the personal contacts he made with other authorities. The Australian Red Cross Society could not have chosen a more capable ambassador.

At the termination of his address, Dr. J. S. Cahill, the President, thanked Dr. Morris for the address and invited Colonel Lennox Speirs to move a vote of thanks and Dr. Ivan Maxwell to support it.

Colonel L. Speirs took the opportunity, as an army medical officer, to pay a tribute to the excellent service given by the Red Cross Society to military medical establishments at home and abroad and at all times. It was the business of the army to set up the bare essentials required for the care of the sick and wounded soldiers, but the Red Cross supplied all the amenities which converted military barracks into pleasant hospitals. He asked Dr. Morris to take notice of his opinion that arrangements should be undertaken by the Australian Red Cross Society on behalf of soldiers away from home to allay their undoubted anxiety concerning the well-being of the wives and small children they left behind them.

Dr. Ivan Maxwell referred more particularly to information supplied by Dr. Morris concerning the way in which the British and American Red Cross Societies put into effect the practice of sending supplementary food parcels to each prisoner of war in enemy hands, the contents of which were calculated scientifically to bring the food value of the dietary up to an amount sufficient for the maintenance of an average adult doing moderately heavy work. Moreover, care was taken to ensure that the parcels contained all the desiderata for a complete diet when added to the components of the food supplied officially in the prison camps.

The vote of thanks was carried by acclamation.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held at the Institute of Medical and Veterinary Science, Adelaide, on August 7, 1942. The meeting took the form of a symposium on "The Production and Distribution of Clean Milk, with Special Reference to Adelaide's Supply". Three papers were contributed.

Dr. H. K. Fry spoke from the medical and public health point of view, and he reviewed the legislation regarding milk in England and South Australia, and gave an outline of the activities of the Metropolitan County Board in the metropolitan area. The average composition of milk revealed by 18,000 examinations carried out in Adelaide by the Director of Chemistry was 12·96, total solids; 4·03, fats; 8·93, solids not fat. Reductase tests of milk samples showed that 4% of the total were unsatisfactory. In recent samples the

average was higher. Tuberculin testing had been carried out by the Government on a limited scale and figures were quoted of results up to the present time.

Miss Nancy Atkinson read a paper on the bacteriology of milk. She stated that pathogenic bacteria might gain access to milk from the cow and from the personnel handling the milk. From diseased cows the tubercle bacillus, staphylococci, streptococci or *Brucella abortus* might enter the milk. From the personnel, if diseased or carriers of disease, the organisms of diphtheria, scarlet fever, acute tonsillitis, dysentery or enteric fever might be introduced to the milk. Environmental bacteria were also generally present, coming mainly from milking utensils inadequately sterilized. As milk was a good culture medium for many species of bacteria, great multiplication would take place if the milk was not well cooled as soon as collected. The best protection from milk-borne infection was afforded by carefully controlled pasteurization followed by immediate cooling and bottling in sterile bottles. Methods of bacteriological examination of milk did not generally include tests for special pathogens, as these organisms were often difficult to detect. Routine tests for the general quality of the milk were used, and these included the breed clump count, the coliform test, and the methylene blue reduction test.

Mr. I. W. McDonald briefly outlined the factors concerned in the production of good quality milk on the farm, and stressed those aspects in which there was most room for improvement. It was pointed out that two-thirds of the milk supplied to the city of Adelaide was produced on farms outside the metropolitan area. Until September, 1941, there were no regulations governing hygiene on these farms and, owing to wartime conditions, there was at present no possibility of enforcing a reasonable application of these legal requirements. At the dairy farm, the most important feature of hygiene was the thorough cleaning and "sterilization" of all utensils; this necessitated the provision of adequate facilities for washing and steam sterilization—facilities which were by no means the rule. The various factors influencing the efficiency of production of milk (per cow, per acre and per unit of labour) were briefly outlined. Other economic factors considered essential were: (*a*) a controlled price to farmers to ensure stability of the dairying industry, (*b*) an adequate return to enable farmers to maintain a reasonable standard of living and to pay a reasonable wage to employees, and (*c*) provision of a cheap source of power for engines, heating and lighting. Finally much work was required in the education of the personnel engaged in this industry, and for this a great increase was necessary in the number of extension workers available to help the farmers.

A MEETING of the Medical Sciences Club of South Australia was held at the Institute of Medical and Veterinary Science on September 4, 1942.

The Fourth Compartment of the Stomach of the Sheep.

Mr. R. H. Watson presented a paper entitled "Intubation of the Fourth Compartment of the Stomach of the Sheep: The pH of its Contents Measured in Situ". Mr. Watson, in describing the results of experiments carried out at the Nutrition Laboratory, said that in the study of the course taken into the stomach by liquid administered into the mouth of sheep, a number of animals were found in which all the liquid consistently passed to the fourth compartment of the stomach (abomasum). Intubation of this compartment was successfully performed by introducing the tube into the œsophagus through the nostril, until the tip was one to two inches proximal to the cardia and then delivering water into the mouth and allowing the tube to pass on with the swallows.

Antimony electrodes had been introduced along with the abomasal tubes and the pH values of the contents determined *in situ*. A series of comparable values which were obtained in this manner from one sheep over a period of several hours were presented. They showed variations from about pH 2 to more than pH 6 over relatively short periods. This variation was attributed to the transfer of rumen contents to the abomasum.

Antibacterial Substances Produced by Microorganisms.

Miss Nancy Atkinson presented a paper entitled "Antibacterial Substances Produced by Microorganisms". Miss Atkinson said that antibacterial substances might be produced by bacteria, both spore-forming and non-spore-forming, by actinomycetes and by fungi. Among the spore-forming bacteria the *Bacillus* group found so frequently in soil, frequently formed the antibacterial substances, some of which had recently been described by Dubos under the names gramicidin and tyrocidin. Both were polypeptides and showed marked inhibitory action towards Gram-positive organisms, tyrocidin also being active against Gram-negative organisms.

Of the non-spore-forming bacteria *Pseudomonas pyocyaneus* produced two active substances, pyocyanin, a green pigment, and pyocyanase, a lipoidal material. The former was very active against some Gram-negative bacilli; the latter acted on a variety of bacteria mainly Gram-positive.

Recent work on the antibacterial substances of *Actinomyces* by Waksman had produced two crystalline substances called actinomycin A and B. Actinomycin A was extremely active against certain Gram-positive bacteria; B was not so active. The latest active substance described by Waksman was called streptothricin and was particularly active against Gram-negative organisms.

Of the antibacterial substances produced by moulds the best known was Fleming's penicillin found in filtrates of cultures of *Penicillium notatum*. It was very active against Gram-positive organisms. Its chemical constitution was unknown, and purified preparations had only recently been obtained by Florey and his colleagues. Another mould product was gliotoxin formed by a species of trichoderma. It was originally described as a fungicide, but had recently been shown to be inhibitory to both Gram-positive and Gram-negative organisms. Other antibacterial substances produced by aspergilli had also been recently described, but no name or chemical constitution had yet been assigned to them. Some of the latest work on mould products was being done by Raistrick, who had just embarked upon a systematic study of the numerous metabolic products described by him during the last decade, for antibacterial activity. So far penicillic acid had been found active against both Gram-positive and Gram-negative bacteria, and citrinin active against Gram-positive bacteria. Both these substances were produced by penicillium species. Although neither substance was as active as penicillin, the yield and ease of isolation of these two substances might well compensate for their lesser activity.

If any of these antibacterial substances were to be of great therapeutic value, they would have to prove non-toxic in the animal body. Animal inoculation tests had shown gramicidin, tyrocidin, actinomycin A and gliotoxin to be highly toxic. Gramicidin, however, was not toxic on local application and showed beneficial effects in a clinical trial on twelve patients infected with Gram-positive organisms. Streptothricin was much less toxic than actinomycin A, and penicillin had been used in large doses by Florey in a limited clinical trial in which great benefit to the patient occurred without any toxic effects. The other substances had not been the subjects of experiment.

The Isolation of a Protein Hydrochloride from Wheat.

Mr. L. S. Walters gave a short account of some recent work which had been done in the United States of America on the isolation from wheat flour of a protein hydrochloride which was toxic for yeast. Mr. Walters said that it had been long known that there existed in wheat and other cereals a substance that inhibited the growth of yeast. This substance had now been isolated in the form of a pure crystalline protein hydrochloride from wheat flour by Balls, Hale and Harris, of the Enzyme Research Laboratory, United States Department of Agriculture.

Wheat flour was extracted with petrol, and the extract was hydrolyzed with alcoholic hydrochloric acid. The hydrolysate was further purified by crystallization from alcohol, giving, finally, the pure protein hydrochloride. The substance was readily soluble in water, and had a molecular weight of about 12,000. Nearly 50% of the total nitrogen was in the form of arginine.

When tested against *Saccharomyces cerivisiæ* the protein brought about the death of the cells in concentrations of 0·005 milligramme per millilitre and higher. It was strongly inhibitory to the growth of the yeast in one-tenth of the above concentration.

Similar results were obtained with pathogenic yeasts, but tests had failed to reveal any fungicidal activity.

Correspondence.

THE SCIENTIFIC EXPERT AND COMMON SENSE.

SIR: I showed your leading article, "The Scientific Expert and Common Sense" (May 1, 1943), to a business man. His comment was: "It's quite true. Doctors are fleeced by 'go-

getters'. They may know medicine, but they have little common sense." I pointed out to him that the reverse holds good. Business men have common sense in money matters, but are fools when it comes to a question of their health.

One half of the world doesn't know how the other half lives. Our lives become centred in ever-narrowing circles, our views so fixed and bigoted that we are unable to appreciate or tolerate the views of others, our associates those with the same views as ourselves. Instead of knowing the lives of one-half of the world we only know the views of fewer and fewer people, who hold the same views as we ourselves.

If this is true of every-day life, how true is it of experts? An expert with specialized training and with no knowledge of the world, is launched forth into the world with views already formed for him by experts, who staunchly follow prevailing traditional trends. It is only the stern reality of defeat after defeat that made the English Army drastically change its organization and methods.

Many revolutionary ideas have been conceived by those who were not experts. Leonardo da Vinci predicted 400 years ago the trends of modern war. An undertaker invented the modern telephone. Pasteur laid the foundations of modern surgery. It, too, is a curious thing that most discoveries have been made by individuals working alone and not in groups. A lone worker has not the assistance of experts to prevent him from wandering off the beaten track to places where vast unexplored treasures await discovery. The active resistance of experts to the revolutionary ideas of warfare proposed by French, English and American writers during the past twenty years, and their subsequent adoption by the Germans, is too recent to need further comment. The active and bitter resistance of medical experts to revolutionary discoveries, even aseptic surgery, may be a tribute to our conservatism, but it emphasizes more the fixity of our ideas.

This is an age of experts, an age when common sense seldom appears. Economists direct our way of life and the economical position is worse than ever. Psychologists and educationalists have applied knowledge of conflicts, complexes, repressions, vocational guidance and the like in the training of children, and the waywardness of modern youth has become a major social problem, and this in spite of the fact that "quality" and not "quantity" children were to be perfect. Experts stress the need of fresh air, vitamins and the wide open spaces. Fifty *per centum* of the population of New South Wales live in Sydney, in cramped flats, designed by experts to give maximum light and ventilation, and their food expertly cooked and prepared is bought in tins. If they have large families (which some experts say are essential if the nation is to survive, whilst others say that the children cannot be properly looked after) and if they are on the basic wage they cannot afford to buy milk and other fresh foods so essential for growing children.

"It is a mad world, my masters"—a world of contradictions, a world of dogmatic assertions and proofs by experts, a world of kinks, fads and fancies. We, the common people, bewildered by it all, make "confusion doubly confounded" by picking out from the bewildering array of plums put in front of us by experts, those that suit us best and hang on to them like grim death and then like jesting Pilate we ask ourselves "What is truth" and will not stay for an answer. Perhaps after all we are no better than the ancients, who were so aptly summed up by Solomon (Ecclesiastes vii, 30): "Only this I have found, that God made man right, and he hath entangled himself with an infinity of questions."[1]

The more one examines the question, the more one must admit that Mr. Bevin and you, sir, have much right on your side.

Yours, etc.,

S. MINOGUE.

Rydalmere,
Sydney,
May 14, 1943.

AN UNUSUAL INJURY TO THE RECTUM.

SIR: The following case history is so unusual that I consider it warrants publication.

H.C., a male, aged forty-nine, was admitted to the Brisbane Hospital at 2 p.m. on March 7, 1943.

At 6 a.m. that morning he put a cow in a yard to be served by a bull. In an adjoining yard was a young dehorned bull. H.C. entered this yard and bent down to attend to the gate with his back to the bull. The bull reared and put its front legs on the gate, pinning him there; the bull's penis then entered his rectum. The trousers he was wearing were old ones, and there was a tear about two and a half inches long in the seat opposite his anus. It is thought that this tear was made by the bull's penis.

He felt little pain at the time and worked in the cow yard for two hours, when he had to desist because of abdominal pain.

On admission to this hospital he exhibited the signs of general peritonitis.

An immediate laparotomy was performed. The abdominal cavity contained much foul black fluid and fæces. There was a tear one inch long in the anterior rectal wall about five inches from the anus. This was oversewn, as much fluid and fæces removed as possible, a left inguinal colostomy performed, and the pelvis and wound drained.

As was to be expected, he only survived twenty-four hours after the operation.

Yours, etc.,

AUBREY D. D. PYE,
General Superintendent.

Brisbane Hospital,
Brisbane,
May 14, 1943.

[1] The quotation is from the Douay version.

THE FUTURE OF MEDICAL PRACTICE.

SIR: All these ingenious schemes for saving the profession from being absorbed into the civil service are quite unnecessary. Is there any service that we cannot now secure for our patients?

In these days of fast aeroplanes distance is but a slight obstacle; if the pathologist or radiologist is needed for aid in diagnosis, is he not there ready and anxious to help? Specialists of all kinds are available and good private hospitals abound. The one and only real difficulty is that the patient may not have enough money to pay for those services.

Now it is simply childish to say that a country has no money for medical service betterment, or for any other purpose, when it has the skill, the men and the material and plant to create that betterment. The Commonwealth Bank can create that money in five minutes just as the private banks have been creating it for centuries.

My plea now is that, instead of promulgating schemes which would tend to drag the profession down to meet the poverty of the people, we band together to help the people to secure the full monetary equivalent of their economic achievements. The effective demand—money—will create the supply—an efficient medical service for all.

If we really believe in democracy we will get away from this eternal "planning" and "scheming" to control the lives of others; we will move away from dictators, directors and their deputies, from the civil service which might easily become the deadly enemy of society, and make some effort to retain the few liberties now left to us.

That can only be achieved by a revolutionary reform of the monetary system. Referring to the present monetary system, Vincent C. Vickers in "Economic Tribulation" states:

> Surely, then, it is commonly felt, it is better that ordinary individuals should leave economics to the economists, finance to the bankers, and national policy to the politicians! But, alas, that is exactly what we have for too long been doing. Look at the result! The experts have hopelessly failed. . . . I still believe that the existing system is actively harmful to the State, creates poverty and unemployment, and is the root cause of war. . . . Moreover, it may be that the present system, which international finance has forced our democratic governments to adopt, uphold and protect by every possible means, has undermined the character of the people and forced them to alter their definition of the word "honesty" so that it may be made to comply more nearly with modern practice.

Vickers should know what he was talking about, for he was governor of the Bank of England from 1910 to 1919 and a director of Vickers, Limited, for twenty-two years.

Nothing could be more absurd than to believe that a satisfactory medical service could be created and maintained within the ambit of a decadent capitalist system, which has reduced the world to something resembling a planetary lunatic asylum in which the majority of those in charge are themselves badly in need of some drastic convulsive therapy to shake them into some sense of reality.

I hope, without any great confidence, that this war will lead to the adoption of a sane social and economic system which will retain all the undoubted advantages of individual enterprise and initiative—a true political and economic democracy.

Yours, etc.,

J. E. STREETER.

Wickham House,
Wickham Terrace,
Brisbane.
May 15, 1943.

THE DISTRIBUTION OF DISEASES IN THE SOUTHERN PACIFIC.

SIR: I have just read in your issue of March 27, 1943, a paper by Captain C. M. Deland entitled "The Distribution of Diseases in the Southern Pacific".

I practised in Suva, Fiji, with one year in western Samoa, from 1931 to 1941 inclusive and cannot agree with some of his statements.

1. He says: "It was doubtful whether measles was the true cause of the enormous number of deaths in Fiji in the eighties." It is a fact that measles was brought to Fiji by the King on his return from Australia. Over 40,000 died in a short time. The native treatment was to get into the sea or river as soon as the temperature rose. Many died of pulmonary complications. Example: I had a patient in Fiji four years ago who treated his measles with cold showers. He finished up with an added bronchopneumonia and cerebro-spinal meningitis (pneumococcal) proved by spinal puncture.

2. Captain Deland says: "For some reason diphtheria did not spread and virulent streptococci were practically absent. Tonsillitis, rheumatism, erysipelas and scarlet fever were not seen." Speaking for Fiji, I can say they are all seen. I have seen diphtheria epidemics there which spread with remarkable ease, and virulent streptococci are always on duty. Three years ago there was a big epidemic of hæmolytic streptococcal sore throat of a very virulent type fortunately relieved by the sulphonamides. Puerperal septicæmia (streptococcic) has always been with them, and before the advent of "M & B 693" *et cetera* very deadly and rapid. And streptococcic septicæmia took many lives and seemed especially deadly to Europeans. Acute rheumatic fever with cardiac complications, tonsillitis, erysipelas and scarlet fever are all there with the tropical diseases with the exception of malaria. In some districts 70% of the people are said to have hookworm. This is at present, after the intensive treatment by the Rockefeller Institute under Dr. S. M. Lambert over years. Tuberculosis finds Fiji a fertile soil. There are no sanitoria there, no wards or beds for tuberculosis in the hospitals, and the Indians and Fijians die on the mats in their little houses, spreading the disease among their families.

In fact I would say that Fiji has all the temperate zone diseases and almost all of the tropical diseases with the exception of malaria. As regards syphilis, yaws which is endemic is said to prevent the syphilis and treatment is the same. And if some American investigators are right and yaws is a form of syphilis, even this latter statement is open to question.

Yours, etc.,

A. E. BOTSFORD DENOVAN, M.D., C.M. (McGill), Medical Officer in Charge, Mobile X-Ray Unit, Commonwealth Health Laboratory, Kalgoorlie, Western Australia.

May 15, 1943.

Post Scriptum.

All statements made by me can be substantiated by the pathological and bacteriological laboratory, Suva Memorial Hospital, a splendidly equipped laboratory.

DIPHTHERIA OF THE SKIN.

SIR: I was interested in your current comment on page 402 of THE MEDICAL JOURNAL OF AUSTRALIA of May 1, 1943, on the subject of diphtheria of the skin.

The suggestion that desert sore and veldt sore and even Australian barcoo rot were due, in at least a considerable number of cases, to diphtheria infection of the skin was made during the course of the 1914-1918 war. This was shown to be wrong as far as barcoo rot (the Australian desert sore) was concerned, and also, if my memory serves me right, in the case of the South African veldt sore.

During the present war a large number of cases of desert sore occurred amongst the British troops in the Middle East. My own son, Major E. J. C. Molesworth, was a regimental medical officer and informed me that he had seen a large number of such sores in the men of his battalion. He informed me that it was often very difficult to get these to heal while the men remained with their unit and were unable to wash frequently, but that the sores cleared up when the patients were sent to base hospitals or when the men were stationed near the sea and could bathe frequently. At my suggestion he asked for an examination as to the presence of diphtheritic organisms in these sores, but received no pathological reports of positive findings in this respect.

Later, I had an opportunity of discussing the matter with one of the pathologists (Major E. B. Jones, I think) who had been attached to an Australian hospital in the Middle East, and this subject came up. I distinctly remember being told that no case of diphtheria of the skin had been found amongst very numerous instances of desert sore occurring in Australian troops in the Middle East. Even the work of the two men mentioned in your article was touched upon in the discussion, and some doubt was cast upon the accuracy of the findings of these investigators, as nothing but diphtheroids and common pyogenic organisms were found by other workers in the same field.

I am writing this to suggest that various pathologists who served with Australian hospital units in the Middle East might inform the readers of THE MEDICAL JOURNAL OF AUSTRALIA as to their opinion of the frequence of diphtheritic sores among the troops in the Middle East.

Yours, etc.,

E. H. MOLESWORTH.

235, Macquarie Street,
Sydney,
May 19, 1943.

A GRASS SEED IN THE LUNG.

SIR: After reading "A Grass Seed in the Lung" in THE MEDICAL JOURNAL OF AUSTRALIA of May 15, 1943, I think I should record a case that occurred in my practice some years ago, and which I have been diffident in reporting on account of its extraordinary nature.

I was called to attend a boy about eight years of age suffering severe pain in the right side of the chest; he had a bad cough and expectoration which his parents told me he had since infancy. I diagnosed a bronchiectatic cavity with an attack of pleurisy. I ordered poultices which gave him relief. A few days later a pustule developed over the site of his pain; a day or two later his mother asked me to see him again as a hair seemed to be sticking out from the pustule. On visiting him I caught the so-called hair in a pair of forceps, and to my surprise I pulled out a complete head of barley grass fully two and a half inches long, quite soft and flexible, coated with lymphy pus. For some years I kept it in formalin. Where did it come from?

On questioning the parents I found that the lad when about three years old had a violent attack of coughing, and seemed as if he would choke. This continued for at least a week, and ever since he had had a constant cough with profuse expectoration. After the removal of the grass head his symptoms cleared up completely.

My only explanation is that the grass head was pushed up the nose or by mouth entered the trachea through the larynx, passed into a bronchus, and eventually found its way to the pleura, and so through the chest wall.

It seems fantastic, but can you offer any other explanation of how it got there and retained its form through all those years?

Yours, etc.,

F. E. LITTLEWOOD, M.B., Ch.B., Dip.L.O.

Warrnambool,
Victoria,
May 19, 1943.

Post Scriptum.

Since sending my letter *re* barley grass seed in the lung, I find the following in "Jackson & Coates", "Bronchiectasis due to Foreign Body", page 1110: In the statistics of the Bronchoscopic Clinic there are quite a number of cases showing that bronchiectasis due to foreign body practically always gets well spontaneously after removal of the foreign body.

FLAVINES AS ANTISEPTICS.

SIR: The following may prove of interest in regard to the increasing use of flavines as antiseptics; it also illustrates the tendency to relapse that exists in some cases after sulphonamide therapy. The patient, a thin man, aged sixty-seven years, was admitted to hospital suffering from influenza and auricular fibrillation. He had an old rheumatic endocarditis. Ten days later, whilst apparently convalescent, he developed pleurisy over the base of the left lung, followed by lobar pneumonia. He was treated with "M & B 693" in full dosage, but his response was slow, and on the twenty-third day after his admission to hospital he developed extensive pleuritic signs over the front of the left lung. On the thirty-fourth day an effusion began to develop at the base of the left lung, and on the thirty-seventh day he had every indication of empyema. However, when aspiration of the chest was carried out, sterile straw-coloured exudate was obtained. The patient then recovered; but on the forty-seventh day he had more pleural pains, and by the fifty-ninth day he had another pleural effusion, despite further treatment with "Dagenan". The diagnosis of empyema was confirmed by paracentesis on the sixty-first day; fairly thick, greenish-yellow pus was obtained, which was found to contain pneumococci in abundance. Operation was refused by the patient, who showed obvious signs of toxæmia. Treatment with "M & B 760" was then instituted, with little improvement. Aspiration was again carried out on the sixty-third and sixty-seventh days. On the seventieth day after aspiration, six cubic centimetres of "Dagenan Soluble" in 50 cubic centimetres of sterile water were introduced into the pleural cavity; the same procedure was repeated on the seventy-second, seventy-fourth and seventy-sixth days. Subsequently a growth of microorganisms from the fluid aspirated was still obtained. On the seventy-ninth day, after aspiration, the cavity was washed out with a 1 in 1,000 solution of acriflavine and 20 cubic centimetres of a 1 in 500 solution of acriflavine were instilled. The procedure was repeated on the eighty-first, eighty-fourth and ninetieth days, and the patient finally recovered. An X-ray examination on the hundred and tenth day revealed thickened pleura at the base of the left lung. The patient was discharged on the hundred and fifteenth day to a convalescent home. Four months later examination of the left lung revealed no evidence of his illness. The only comment the patient made was that he had "spat up yellow stuff for a few weeks"; this was evidently acriflavine passing through the lymphatics of the lung to the alveolar secretion, in which it was expectorated.

I am indebted to Dr. Dawes, of Orange, for the pathological examinations. He found that the straw-coloured inflammatory exudate which was obtained on the thirty-fourth day of the patient's illness contained some cells—neutrophile cells and lymphocytes; very few erythrocytes were present. Dr. Dawes stated that he had encountered similar findings in a number of cases in which "M & B 693" had been given, and in which the patients might have developed empyema without "M & B 693" therapy. A smear from material taken on the sixty-first day contained pus cells and pneumococci; pneumococci were grown on culture. The findings in material taken on the sixty-third day were similar to those of the sixty-first day. Material taken on the seventy-fourth day, after treatment with "Dagenan Soluble" had been given, still yielded a growth of pneumococci. Fluid taken on the seventy-ninth day, after two trials of acriflavine therapy, yielded a profuse growth of a Gram-negative bacillus, which Dr. Dawes thought was possibly Friedländer's bacillus; no pus cells were seen. On the eighty-fifth day, after two further sessions of acriflavine therapy, the pleural fluid was found to contain one or two pus cells in an amorphous thick fluid, and no organisms were grown on attempted culture from it.

Yours, etc.,

F. J. KELLEHER.

"Carmel",
Templar Street,
Forbes.
May 28, 1943.

OMISSIONS FROM TEXT-BOOKS.

SIR: Two points in Dr. Jessie B. Simpson's letter in the current issue of THE MEDICAL JOURNAL OF AUSTRALIA call for comment.

Her advocacy of the so-called "safe period" (what she calls "the self-control theory of birth control") is unduly enthusiastic. I have seen several hundred pregnancies result from intercourse limited so as to exclude what she calls "the dangerous phase from the ninth to seventeenth days". The so-called safe period is very unsafe indeed.

She states "that the use of rubber contraceptives is extremely likely to greatly increase the incidence of carcinoma of the cervix". What grounds has she for this assertion? Experience of hundreds of thousands of cases at birth control clinics in England and America, as well as the experience of tens of thousands of cases by individual gynæcologists, affords no ground whatever for such a statement.

While the use of rubber contraceptives is not likely directly to decrease the incidence of carcinoma of the cervix, it is likely to do so indirectly, since the patient who is fitted with a rubber contraceptive by a gynæcologist is subjected to a gynæcological examination, at which diseased conditions predisposing to carcinoma of the cervix are likely to be detected and treated in good time.

The "moral" bias, which is evident in the letter, has unfortunately led its writer to abandon the scientific objectivity which is desirable in the discussion of medical subjects, however controversial they may be.

Yours, etc.,

NORMAN HAIRE.

193, Macquarie Street,
Sydney,
May 28, 1943.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Numbers 102, 107 and 113, of May 13, 20 and 27, 1943.

PERMANENT NAVAL FORCES OF THE COMMONWEALTH (SEA-GOING FORCES).

Appointments.—James Richard David Cotton and William Ronald Thompson are appointed Temporary Surgeon Lieutenants (D), dated 19th April, 1943, and 2nd May, 1943, respectively.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

Pilot Officer D. C. Swan (6871) is transferred from the Administrative and Special Duties Branch with effect from 1st January, 1943, with present rank and seniority.

The probationary appointment of Pilot Officer D. C. Swan (6871) is confirmed and he is promoted to Flying Officer with effect from 1st January, 1943.—(Ex. Min. No. 117—Approved 5th May, 1943.)

Flight Lieutenant D. T. Shortridge (1472) is granted the acting rank of Squadron Leader whilst occupying a Squadron Leader post with effect from 25th July, 1942.—(Ex. Min. No. 119—Approved 5th May, 1943.)

The following temporary Squadron Leaders are promoted to the temporary rank of Wing Commander, with effect from 1st April, 1943: J. A. Game (1216), W. McL. Borland (1477), W. M. Lemmon (1284), F. G. Steele (1601), A. J. W. Ahern (1884).

The following Flight Lieutenants are promoted to the temporary rank of Squadron Leader, with effect from 1st April, 1943: N. L. Newman (1890), H. M. Webber (1893), A. E. Kahn (2061), J. A. Horan (2570), J. S. Burgess (1372), L. L. O. Bevan (2860), A. E. Dickmann (2396), I. L. Miller (1230), A. L. Kennett (1528), E. J. Davies (1504), J. M. Alexander (1669), A. C. Blumer (1469), B. Epstein (1714), J. H. Deakin (1767), W. B. Marsh (1768), C. V. W. Brown (1467), N. W. Martin (2869), R. G. Baker (2574), R. E. Ashbarry (3724).

Temporary Squadron Leader M. L. Creightmore (1210) is promoted to the temporary rank of Wing Commander with effect from 1st April, 1943.

The following Flight Lieutenants are transferred from the Reserve for full-time duties with effect from 5th April, 1943: James Ballard Felstead (7109), James Lawrence Sinclair (7225), James Howard Stewart Waters (7226).

The following Flight Lieutenants are transferred from the Reserve, with effect from 5th April, 1943: J. B. Foster (257222), H. G. Hiller (256811), W. B. MacDonald (256798), G. A. Robbie (256865), H. R. Thomson (256874), V. W. Threlkeld (256829), V. G. Walker (256955).

Squadron Leader J. J. Arnold (1848) is granted the acting rank of Wing Commander whilst occupying a Wing Commander post, with effect from 22nd February, 1943.

The following Flight Lieutenants are granted the acting rank of Squadron Leader whilst occupying Squadron Leader posts, with effect from the dates indicated: J. F. Hughes (2290), 15th February, 1943; A. E. Dickmann (2396), J. W. L. Price (2118), 1st February, 1943; J. Helms (2864), 25th February, 1943.—(Ex. Min. No. 138—Approved 19th May, 1943.)

Pilot Officer D. C. Swan (286871) is granted the acting rank of Flight Lieutenant whilst occupying a Flight Lieutenant post with effect from 1st February, 1943.

Reserve: Medical Branch.

The following are appointed to commissions on probation with the rank of Flight Lieutenant, with effect from the dates indicated: Thomas Harold Vickers, M.B., B.S. (267428), 17th March, 1943; Torry Ernest Hester Spark, M.B., B.S. (267437), 26th March, 1943; Peter Wilkinson Read, M.B., B.S. (257475), Peter Reay Bull, M.B., B.S. (257476), John Patrick Walsh, M.B., B.S., B.D.Sc., L.D.S. (257477), George Russell Jones, M.B., B.S. (257478), Robert William Edward Manser, M.B., B.S. (257479), 19th April, 1943.—(Ex. Min. No. 132—Approved 19th May, 1943.)

CASUALTIES.

ACCORDING to the casualty list received on April 28, 1943, Lieutenant-Colonel F. R. Hone, A.A.M.C., Adelaide, South Australia, has been "placed on and removed from the 'seriously ill' list".

Obituary.

ERNEST HARRIS BEAMAN.

WE regret to announce the death of Dr. Ernest Harris Beaman, which occurred on April 11, 1943, at Yeppoon, Queensland.

Australian Medical Board Proceedings.

QUEENSLAND.

THE undermentioned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in medicine:

Booth, Frederick John, on active service.

The undermentioned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in surgery:

Nicholson, Alphonso Jean Gardiner, 584, Ipswich Road, Annerley.

The undermentioned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in tropical diseases:

Fryberg, Abraham, on active service.

The undermentioned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in ophthalmology:

Bennett, Aubrey George, 76, Charters Towers Road, Townsville.

The undermentoned has been registered, pursuant to the provisions of *The Medical Acts*, 1939-1940, of Queensland, as specialist in gynæcology and obstetrics:

Leeds, Robert Harvey, Biloela.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Grieve, Percy Neil, M.B., 1915 (Univ. Sydney), Walgett Street, Collarenebri.

Medical Appointments.

Dr. Horace Joseph Carlyle Edmonds, pursuant to the provisions of the *Lunacy Acts* of Victoria, has been appointed Superintendent (acting) of the Mental Hospital, Ballarat.

Dr. James Campbell Moffatt has been appointed Acting Government Medical Officer at Cairns.

Diary for the Month.

JUNE 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JUNE 8.—Tasmanian Branch, B.M.A.: Branch.
JUNE 11.—Queensland Branch, B.M.A.: Council.
JUNE 15.—New South Wales Branch, B.M.A.: Ethics Committee.
JUNE 16.—Western Australian Branch, B.M.A.: Branch.
JUNE 17.—New South Wales Branch, B.M.A.: Clinical Meeting.
JUNE 22.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JUNE 23.—Victorian Branch, B.M.A.: Council.
JUNE 24.—New South Wales Branch, B.M.A.: Branch.
JUNE 24.—South Australian Branch, B.M.A.: Branch.
JUNE 25.—Queensland Branch, B.M.A.: Council.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 235, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

Editorial Notices.

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All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility unless such a notification is received within one month.

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